Martha L. Sternberg

From her affectionate husband

Geo. H. Sternberg

San Francisco

Dec. 4, 1891

REPORT

UPON THE

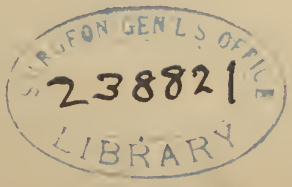
PREVENTION OF YELLOW FEVER BY INOCULATION,

MADE IN COMPLIANCE WITH INSTRUCTIONS FROM THE PRESIDENT OF THE UNITED STATES, AND IN ACCORDANCE WITH AN ACT OF CONGRESS PROVIDING FOR THE CIVIL EXPENSES OF THE GOVERNMENT FOR THE YEAR ENDING JUNE 30, 1888.

SUBMITTED IN MARCH, 1888,

BY

GEORGE M. STERNBERG,
MAJOR AND SURGEON, U. S. ARMY.



ORDERS.

WASHINGTON, *April* 29, 1887.

SIR: Referring to the act providing for sundry civil expenses of the Government for the year ending June 30, 1888, especially to the clause providing for the investigation of yellow fever by inoculation, as follows: "And the President is further authorized to use of the same unexpended balance a sum not exceeding $10,000 for the purpose of investigating the merits of the method practiced in Mexico and Brazil for preventing yellow fever by inoculation," you are hereby directed, under the authority of said act, to proceed to Rio de Janeiro, where you will collate the documentary and other evidence of the experiments by Dr. Freire. Having thoroughly familiarized yourself with the claims of Dr. Freire, you will proceed in person to inquire at the Jura-Juba Hospital, and such other places as may occur to you after your arrival at Rio—

First. The source from which the culture supply is secured, which will involve—

(*a*) The examination of the alleged germ as shown you by those engaged in the business of inoculation.

(*b*) Verification of the cultivation and process of attenuation adopted.

Second. The method of the inoculation, which you will see verified, if practicable, on actual cases.

Third. You will report your opinion on the results attained by the process after a careful examination of the cases which have previously been subjected to inoculation. In forming your judgment of these results you will take into consideration the following points:

(*a*) Personal characteristics of the patient; age, race, nativity, sex, previous susceptibility.

(*b*) The period since last inoculation; number of times exposed to the contagion.

Having completed this study, you will then proceed to Mexico by the shortest and most practicable route and investigate, in the same manner, the method of inoculation practiced by Dr. Carmona y Valle, and the same method will be observed in conducting the investigation.

While your attention is directed specifically to these points and details, with the expectation that they will be carefully kept in view and adopted for your guidance, they are not intended to exclude such additional methods and means of investigation as your judgment may approve in the thorough and careful accomplishment of the purposes of your mission.

In order that every facility may be afforded you for the prosecution of the work, you will make known your errand to the United States minister at Rio de Janeiro and the United States minister at the city of Mexico, respectively, and request them to use their influence in procuring such access to the hospitals and such other sources of information as you may desire. You will refrain from making publication of your investigations and the conclusions reached by you until you shall have submitted to

me the completed report. You will forward your vouchers for traveling expenses, from time to time, to the Supervising Surgeon-General of the Marine-Hospital Service for payment, certifying the same before any consular officer where you may be at the time.

You will also make requisitions on the Supervising Surgeon-General for such scientific appliances as may be necessary to accomplish the object of your journey.

It is expected that your investigation will be completed by the 1st of October.

GROVER CLEVELAND.

Maj. GEORGE M. STERNBERG,
Surgeon, U. S. Army.

LETTER OF TRANSMITTAL.

BALTIMORE, MD., *March* —, 1889.

To the PRESIDENT:

I have the honor to transmit herewith a detailed report of the investigations which I have made in compliance with your instructions dated April 29, 1887.

The conclusions reached are definite so far as the methods of inoculation practiced in Brazil and in Mexico are concerned; but, unfortunately, the question of the etiology of yellow fever is left in an unsettled state.* The limit as to time fixed by my orders, and the fact that the disease was not prevalent either in Brazil or in Mexico at the time of my visits to those countries made it impossible for me make certain researches which I consider extremely important in connection with the subject under investigation.†

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Very respectfully, your obedient servant,

GEO. M. STERNBERG,
Major and Surgeon, U. S. Army.

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* The question of etiology was not included in the law, which only contemplated the study of the method practiced by MM. Freire and Carmona y Valle. Dr. Sternberg is understood to be engaged at present in the separate study of the etiology of yellow fever, under authority of a subsequent executive order.—ED.

† Since this report was submitted the writer has made extended researches in Havana, Cuba, during the summers of 1888 and of 1889, and in Decatur, Ala., during the epidemic of last year. The results of these researches will be embodied in a report to be submitted hereafter. For the present it suffices to say that these results fully confirm the conclusions reached in the present report with reference to the claims of Dr. Domingos Freire, of Brazil, or of Dr. Carmona y Valle of Mexico, to have discovered the specific infectious agent in the disease under investigation—*i. e.*, that these claims have no scientific foundation.

BALTIMORE, *September* 20, 1889.

PREFACE.

Having for some years been deeply interested in questions relating to the etiology and prophylaxis of the infectious diseases, and particularly of yellow fever, the writer was glad to undertake the investigation to which the following report relates, especially as it would give him a long-sought opportunity to supplement observations made in Havana, in 1879, by additional experiments, made by methods which have been perfected since that date. It must be admitted that the published works of Dr. Freire, in Brazil, and of Dr. Carmona y Valle, in Mexico, did not inspire him with much confidence as regards the scientific value of the alleged discoveries made by these gentlemen; but while it was evident from their writings that they had fallen into gross errors, the possibility remained that there was a germ of truth in the background. The published statistics of Dr. Freire, especially, were so favorable to his claim that he had discovered a method of prophylaxis by inoculation that a critical examination upon the spot was evidently the only way of ascertaining the exact value which should be accorded to these statistics.

It is always an ungrateful task to criticise the work of those who have earnestly and conscientiously sought to elucidate unsettled questions in science, and especially so when the object in view is the amelioration of human suffering. It would have been extremely gratifying to the writer if he had been able to announce as the result of his investigations that the specific germ of yellow fever has been discovered in Brazil or in Mexico, and that a reliable method of prophylaxis by inoculation is now successfully practiced in one or the other of these countries. Such a report would be easily written and gladly received by the medical profession in this country and in Europe; but unfortunately I am unable to make a favorable report, and to sustain a negative and show wherein the gentlemen above named have, in my opinion, been mistaken, calls for an elaborate and extended statement of facts, which I am aware will have but little interest for a majority of the profession; but those who do take the pains to read it will find, I trust, that I have fully sustained the positions taken; and for those who in future may undertake to elucidate the unsettled questions relating to the etiology of yellow fever, the report will be found, I believe, a useful beacon, showing the rocks and quicksands in the way of the investigator in this field of science, and the absolute importance of proper training and familiarity with modern methods, and with the results of the most recent researches, before entering upon a path in which so many pioneers have gone astray.

REPORT UPON THE PREVENTION OF YELLOW FEVER BY INOCULATION.

INTRODUCTION.

At the annual meeting of the American Public Health Association, held in Washington in the month of December, 1885, resolutions were introduced by Dr. Joseph Holt, president of the Louisiana State board of health, calling for the appointment of a commission by the National Government for an investigation of the merits of the protective inoculations against yellow fever which had been practiced in Brazil and in Mexico.

These resolutions were adopted by the association, and, through the influence of Dr. Holt, upon the assembling of the Forty-ninth Congress a bill was introduced providing for a commission of three members, and an appropriation of $25,000. This bill passed the Senate but met with some opposition in the House, and was subsequently modified to meet the views of a minority of the Committee on Commerce, to which it had been referred. As modified the bill received the unanimous approval of this committee and was again reported to the House by Hon. R. C. Davis, of Massachusetts, to whom it had been referred as a subcommittee. Under the rules it could not be considered except by unanimous consent, and the opposition of a single member prevented it from being submitted to a vote. During the next session of Congress a clause was introduced into the act providing for the sundry civil expenses of the Government for the year ending June 30, 1888, appropriating $10,000 for the investigation. This appropriation was secured mainly through the exertions of Dr. Davis, and the active interest of the Louisiana delegation in Congress.

The President designated the writer to carry out the investigation referred to, and by special orders from the War Department I was directed to report to the honorable Secretary of the Treasury, and received through him detailed instructions (p. 135–6) signed by the President.

In compliance with these instructions I sailed for Rio de Janiero, per steamer *Alliança*, on the 4th of May, 1887, taking with me a complete "field outfit" for bacteriological investigation. I took with me a series of first-class objectives, including the one-eighteenth inch and one-twelfth inch homogeneous oil immersion lenses of Zeiss, which I have found to be unsurpassed for bacteriological researches, and have had in almost constant use since 1879, when they were purchased for the use of the Havana Yellow Fever Commission. I was able to start by the first steamer which sailed after I received my instructions, because my preparations had for the most part been made some time before. In anticipation of the passage of the bill before Congress in 1886, and having been assured by those who were interested in its passage that it was their desire that I should make the investigation contemplated, I made my preparations for field work during the months of May and June of that year, and the boxes containing my apparatus and sterilized culture material had remained packed since

that date. I had provided a large supply of flesh-peptone gelatine, of agar-agar, and of *bouillon* in hermetically sealed tubes, which having been thoroughly sterilized and being secure from injury by drying of the culture-medium, could be preserved indefinitely.

The voyage to Rio occupied twenty-seven days; the steamer touching during the passage at the islands of St. Thomas and Barbadoes, and at Para, Maranham, Pernambuco, and Bahia, sea-ports of Brazil.

Upon my arrival in Rio I at once presented my credentials to the Hon. Thomas J. Jarvis, United States minister and envoy plenipotentiary to Brazil. I was received with great courtesy, and Governor Jarvis subsequently did everything in his power to further the object of my mission, and to make my stay in Brazil as agreeable as possible. Minister Jarvis presented me soon after my arrival to the Baron Cotegepe, prime minister of the Empire, and later I was presented at court to the Princess Isabella, Regent of the Empire during the absence of her august father, Dom Pedro II.

Dr. Domingos Freire, whose claims I had come especially to investigate, was absent in Europe at the time of my arrival. He had gone to France some time previously for the purpose of demonstrating his yellow-fever germ, and calling attention to his method of prophylaxis. I was, however, immediately after my arrival, installed in his laboratory in the school of medicine by the director of the faculty, and received the assistance of his former assistants and pupils, Dr. Chapot Prévost and Dr. Joaquim Caminhoa, to whom I express my obligations, as also to the father of the last-named gentleman, Conselliero Caminhoa, who called upon me immediately after my arrival and made offers of his services in any way that I might desire. These gentlemen were ardent advocates of the method of inoculation practiced by Dr. Freire, and believers in his *cryptococcus xanthogenicus*. I subsequently learned that in this regard there were two parties in Rio, and that the question had been very freely discussed both in the newspapers and in the Imperial Academy of Medicine, in the printed bulletin of which a complete record of their discussions was preserved.

So far as I could learn, the leading and more experienced members of the profession were for the most part extremely skeptical as to the reliability of the alleged discovery and method of prophylaxis, or fully convinced that the claims of Dr. Freire were without foundation, and outspoken critics of his methods and statistical results. On the other hand, Dr. Freire had a certain following among the younger members of the profession, and especially among the medical students, and was looked upon by these as "the Pasteur of Brazil." The very severe criticism which he had received at the hands of certain prominent members of the Imperial Academy of Medicine was looked upon by his personal friends as the persecution which it is so often the fate of discoverers to encounter at the hands of conservative and jealous confrères.

In 1885, when Dr. Freire published his elaborate work, "Doctrine Microbienne de la Fièvre Jaune" at the expense of the Government, he was president of the central board of public hygiene, and seems to have had the full support of the Government in his attempts to elucidate the etiology of the endemic pestilence which interfered so largely with the development of the capital city of the empire. Two assistants of his selection were assigned to him and money seems to have been expended freely in his experimental researches and publications. At the time of my visit to Rio Dr. Freire was no longer in special favor with the Government, and the central board of public hygiene was composed of men who were not favorable to his method of inoculation, and indeed included the names of some of his most vigorous and successful critics. Prominent among these was Dr. Aranjo Góes, a gentleman who was of great assistance to me during my stay in Brazil. At my first interview with the prime minister, the Baron Cotegepe, the name of Dr. Góes was mentioned as one who enjoyed the confidence of the Government, and who had given much attention to the study of the disease I had come to investigate. I found Dr. Góes to be an extremely well-informed physician, a competent microscopist, and one of the pioneers in Brazil in bacteriological studies, especially with reference to yellow fever. He has been

prudent enough not to publish prematurely the results of his investigations, but has made extended experimental studies, and has especially devoted himself to the microscopical examination of sections of the various organs, made *secundum artem*, and stained with various aniline dyes, a method which Dr. Freire seems to have neglected entirely, for neither himself nor his pupils exhibited to me a single mounted preparation showing the "*Cryptococcus xanthogenicus*" in the tissues, or in blood obtained from the victims of yellow fever. Nor did I find in Dr. Freire's laboratory any pathological material preserved in alcohol, for the purpose of histological study. On the contrary, I am indebted to Dr. Góes for material from quite a number of cases, in which he had himself made the autopsy. Although in feeble health Dr. Góes still devotes much of his time to microscopical studies, in the physiological laboratory of the National Museum, which is in charge of Dr. J. B. de Lacerda. The last-named gentleman also gives much time to bacteriological studies, and is especially engaged at present in the study of beri-beri, a disease which prevails extensively on the littoral of Brazil from Rio de Janeiro northward. I desire to express here my obligations to Dr. Lacerda for numerous favors, and especially for having made me at home in his laboratory, where I found a culture-oven in operation and where a considerable part of my work while in Brazil was done.

Dr. Góes was of the greatest assistance to me during my entire stay in Brazil. He went with me to the hospitals in search of yellow-fever patients, and aided me in collecting blood for microscopic examination and culture experiments. The yellow-fever season was about at an end when I arrived in Brazil, but I was fortunate enough to find a few typical cases and to obtain specimens of blood—drawn from the finger—for study. But, although several of these cases terminated fatally, I did not succeed in obtaining an autopsy. This was due to the fact that as soon as the diagnosis of yellow fever was established in a case in the wards of the Misericordia Hospital, or elsewhere in the city, the patient was at once transferred to the small-pox hospital, the Jurajuba Hospital, designed especially for the reception and isolation of yellow-fever patients, having been closed at the end of the epidemic season. I followed two cases to the small-pox hospital, and collected blood from the finger of one whom I found in a ward with ten or fifteen variola patients, and who ejected black vomit in my presence. I was extremely anxious to obtain an autopsy in this case for the purpose of making cultures from blood obtained from the heart and from material from the interior of the organs in which the principal pathological lesions are found, but, unfortunately, did not receive notice of the man's death until he was already buried. This also occurred in another fatal case, notwithstanding the fact that I made every effort to receive immediate notice of the fatal termination of these cases; and in a fatal case at the Misericordia Hospital Dr. Góes and myself arrived just ten minutes too late for an autopsy, the body having already been sent to the cemetery, although the man had been dead but an hour.

The epidemic season in Rio commences usually in December and extends to the last of April. The following table shows the mortality by months from the 1st of January, 1886, to the 1st of May, 1887, during which period a very complete monthly bulletin of mortality statistics has been published by the Inspectoria Geral de Hygiene. In parallel columns I have placed the mean temperature for the month, and the total amount of rainfall in millimeters and in inches.

Month.	Yellow fever.	Mean temperature.		Total rainfall.	
	Mortality.	C.	Fahrenheit.	Millimeters.	Inches.
1886.		°	°		
January	135	25.3	77.5	26.2	1.03
February	234	24.6	76.3	278.1	10.94
March	347	25.3	77.5	76.9	3.02
April	220	23.9	75.0	223.9	8.81
May	48	20.7	69.2	8.9	.35
June	18	19.6	67.3	42.8	1.68
July	9	18.6	65.5	39.4	1.55
August	2	18.6	65.5	136.5	5.37
September	0	20.3	68.5	116.7	4.59
October	1	20.7	69.2	35.0	1.37
November	0	22.7	72.9	35.0	1.37
December	1	23.4	74.1	226.7	8.92
Total	1,015	.....	.....	.....	49.00
1887.					
January	6	25.6	78.1	233.8	9.20
February	16	25.3	77.5	76.4	3.00
March	19	24.3	75.7	205.8	8.10
April	22	23.3	73.9	114.3	4.49

It will be seen from this table that while there was a considerable epidemic in 1886, which terminated, as usual in the month of May, the year 1887 has been characterized by a remarkable exemption from the ravages of the endemic scourge. We can not account for this on the ground of a lower temperature during the epidemic season, for in fact the average temperature for the month was higher in January and February, 1887, than in the corresponding months of 1886. During the months of March and April, however, the temperature was somewhat lower in 1887. The total rainfall for the four months was about the same. The year 1885 was also one of comparative exemption from yellow fever, the total number of deaths having been but three hundred and seventy-five. In a disease which finds its victims for the most part among unacclimated strangers, the mortality will of course depend largely upon the number of new-comers who are exposed to the epidemic influence. This is doubtless one of the principal causes of the fluctuation in the mortality curve from year to year. Not only does a large portion of the susceptible population suffer an attack during an epidemic, and thus enjoys subsequent immunity, but the large mortality induces strangers to avoid the infected city during the following epidemic season. Again an epidemic serves as a stimulus to the local health authorities, and more attention is given to the sanitary police of the city.

All Brazilian authorities agree that yellow fever was first introduced into Rio in the year 1849, but there is reason to believe that it had prevailed in Pernambuco as far back as 1686.

The Portuguese author, Sebastião da Rocha Pitta, has given an account of this epidemic in his "History of Portuguese America," published in Lisbon in the year 1730. This author says (Book VII, p. 427, *et seq.*):

"These disturbances were in Pernambuco the first presages of the fatal disease *Bicha*, and soon after of the dreadful eclipse of the moon, which was witnessed with horror in that province, and in that of Bahia.

In the month of December, 1685, the presiding luminary of the night appeared all ablaze, as if it had concentrated within its service the whole region of fire, the greater part of its immense surface being enveloped in this seeming cloak of flames. Some months before there had been an eclipse of the sun, which was surrounded by a mist, called by a celebrated astrologer, the jesuit father Valentin Extancel, 'the sun-spider."

"On these two eclipses the priest wrote a mathematical treatise, in which he predicted great calamities for Brazil. It is true that eclipses are natural, being caused by

the earth, which enters the orbits of the two greater planets, but through these phenomena the air, from known or hidden causes, may be corrupted and from its corruption result diseases, if not in all the world, at least in some parts of it, as has been shown by the plagues and calamities, of which there are many examples preserved in traditions and writings, and others still fresh in the memory of persons now living.

"*Year* 1686.—In the year 1686 commenced in Pernambuco that terrible plague (contagious disease *Bicha*) which must be attributed to the sins of the population of these provinces, corrupted by vices into which they were enticed by the wealth and freedom of Brazil. Many causes are alleged, the most worthy of attention being the arrival of some barrels of meat which returned from the island of São Thomé. These were opened by a cooper who shortly afterward fell dead. Soon after several persons of his family, to whom he had communicated the disease, also died. The epidemic spread to such an extent among the inhabitants of Recipe (Pernambuco) that the mortality exceeded two thousand, which was very large in proportion to the population.

"Thence the disease extended to Olinda and its vicinity, and very few were the persons who escaped it, such was its virulence and intensity. The variety of the symptoms puzzled the medical profession whose members could only agree on one point, that of giving it the name *Bicha*. Few patients recovered, and numberless were those who died. The deserted hearthstones and the families deprived of their protectors attested the ravages of the disease."

The historian mentions certain clinical features of the disease, to which he refers, which make it appear extremely probable that the epidemic malady described by him under the name *Bicha* was nothing more nor less than yellow fever, but we have no further account of the prevalence of this disease upon the coast of Brazil until quite a recent date.

The highest medical authorities in Brazil agree that yellow fever was not endemic in the principal seaports of the empire prior to the year 1849, when it was introduced to the city of Bahia by the North American brig *Brazil*, which sailed from New Orleans, where yellow fever was prevailing, and touched at Havana. Two of the crew of this brig died of yellow fever during her voyage from the latter port to Bahia. Soon after her arrival the disease made its appearance among those who had communicated with the ship, and later on other vessels in the harbor. The first case occurred a few days after the arrival of this brig (November 3). A part of her cargo is said to have consisted of little barrels of beef which had become putrid. From Bahia the disease was carried to Rio Janeiro, where during the epidemic season of 1850 it caused a mortality of 4,160.

According to Professor Barata, of the Faculty of Medicine of Rio Janeiro, yellow fever continued to prevail in Brazil until the year 1861, when it disappeared for eight years, to re-appear in 1869–'70, as a result of a fresh importation. The Italian ship *Creolla del Plata*, which had touched at St. Iago, where yellow fever was prevailing, is named as the vessel which introduced the disease on this occasion.

The mortality from the disease under consideration in the city of Rio, from the time of its introduction in 1850 to a recent date, is shown by the following table:

Year.	Mortality.	Year.	Mortality.	Year.	Mortality.	Year.	Mortality.
1850	4,160	1860	1,249	1869	274	1878	1,174
1851	475	1861	247	1870	1,117	1879	974
1852	1,943	1862	12	1871	8	1880	1,433
1853	853	1863	0	1872	102	1881	219
1854	21	1864	0	1873	3,659	1882	95
1855	0	1865	0	1874	859	1883	1,336
1856	0	1866	0	1875	1,292	1884	618
1857	1,425	1867	0	1876	3,317	1885	278
1858	800	1868	0	1877	282	1886	1,015
1859	500						

In 1855 yellow fever is said, by Hirsch, to have prevailed extensively in Brazil, although this was not an epidemic year in Rio Janeiro. The following year it extended along the Amazon far into the interior of the country. The years of greatest epidemic prevalence since that date have been 1859–'60, 1862, 1869–'70, 1872–'73, 1875–'77 (Hirsch).

From Brazilian ports the disease has occasionally been introduced to the cities at the mouth of the Rio de la Plata, and has there caused great loss of life. The first epidemic at Montevideo was in 1857, and it was again introduced into this city, from Pernambuco, in 1872. It prevailed in the city of Buenos Ayres in 1858 and in 1870.

We have already stated that the year 1886 was considered an epidemic year, the total mortality having been 1,015. It will be of interest to compare with this figure the mortality from certain other diseases, for the same period. We obtain the following from the official bulletin already referred to:

	Mortality.
1. Tuberculosis	2,077
2. Diseases of the circulatory apparatus	1,458
3. Diseases of the cerebro-spinal apparatus	1,345
4. Diseases of the digestive apparatus	1,097
5. Malarial diseases	1,086
6. *Yellow fever*	1,015
7. Diseases of the respiratory apparatus	988

(Variola 164, typhoid fever 114, beriberi 67.)

It will be seen that so far as the general population is concerned, yellow fever is a disease of minor importance, inasmuch as, even in an epidemic year, it takes the sixth place among the causes of death enumerated. But the mortality from this disease being almost exclusively among the foreign population it is a matter of prime importance to strangers visiting the capital of Brazil, to the commercial interests of the city, and the general development of the country by immigration.

The population of Rio is estimated, in recent official reports, at 400,000, and the total mortality, upon this basis, was 30.75 per thousand during the year 1886, while the mortality from yellow fever was 2.54 per thousand. The total mortality is certainly excessive for a city so favorably located, and no doubt could be very much diminished by the execution of needed sanitary improvements, and by a more rigorous sanitary supervision of the city. It is not too much to say that by well executed sanitary measures the endemic plague so fatal to strangers could probably be entirely banished from this beautiful city, which is so highly favored by its situation and surroundings.

Dr. Freire returned from Europe about the 1st of July, and on the 4th I met him by appointment in his laboratory, where from this time until my departure from Brazil I was a constant visitor, and where he undertook to demonstrate to me the specific character of the micrococcus, which he presented to me as his yellow fever *microbe*, by a series of experiments upon animals, which are detailed in the body of my report.

I desire to express my thanks to Dr. Freire for his uniform courtesy and for copies of his various publications, and for the assistance rendered me in various ways in the pursuit of the object of my mission. Dr. Freire is entitled to much credit for the zeal and perseverence with which he has pursued his experimental studies for a number of years; and if, as I believe, he has fallen into serious errors, it must be remembered that he is not alone in this particular, and that, especially in this field of investigation, many men well known as pathologists, chemists, etc., have been led quite as far astray. Indeed, reliable methods of investigation are of such recent date that the records of work done a few years since in various parts of the world abound in errors of observation and of inference which would at present be inexcusable. The remarks just made apply as well to the work of Dr. Carmona y Valle, of Mexico, who, as I shall show in the body of my report, has fallen into errors of the same kind.

Dr. Freire's laboratory is equipped for the most part with apparatus of French manufacture, including the *étuve d'Arsonval*, and his cultures prior to his departure

for France had evidently been made for the most part, if not entirely, in Pasteur flasks—*petits ballons*. In three closets, respectively, labeled "Cholera," "Cancer," and "Yellow fever," were numerous flasks containing fluid cultures. I was subsequently informed by him that his stock for his cholera cultures came from Dr. Ferran, of Spain, and that his cancer closet contained cultures obtained by himself from cases of cancer. Soon after my arrival Dr. Freire's principal assistant in his bacteriological work, Dr. Chapot Prévost, selected from the yellow fever closet a flask dated February 13, 1885, which he believed to contain the *cryptococcus xanthogenicus*. A biological analysis of the contents of this flask, made by means of Esmarch's tubes, showed that it contained several different bacilli, but no organism corresponding with Dr. Freire's description of the yellow fever microbe. I had previously made a biological analysis of some of the vaccine used by Dr. Freire in his inoculations, which was brought to the United States in a sealed glass tube by Dr. Lane, an American, who has resided for many years in Brazil. This came to me through the courtesy of Dr. Chisholm, of Baltimore, and Prof. William Welch, of Johns Hopkins University. This also contained several different organisms, but none that I could identify with the *cryptococcus xanthogenicus*. Dr. Freire's laboratory was not provided with Koch's culture apparatus, or with the Zeiss homogeneous immersion objectives, but he had a good French stand and an immersion No. 10 of French manufacture. Upon Dr. Freire's return from France he brought with him some cultures in agar-agar which were evidently a novelty in his laboratory. This collection included *Bacillus prodigiosus*, commonly called micrococcus prodigiosus; *Rosa hefa*, the bacillus (micrococcus) of fowl cholera, and of rabbit septicæmia, and two or three other well-known organisms. It also contained a tube said to be a pure culture of the yellow fever microbe, which, to my surprise, proved to be a micrococcus not differing in its morphology from certain well known and widely distributed *forms—c. g., Staphylococcus pyogenes albus*. Details with reference to experiments made with this coccus will be found in my report.

A considerable portion of my time while in Rio was devoted to an investigation of the results of the protective inoculations practiced by Dr. Freire in 1884, 1885, and 1886, and in personally visiting the *corticos*—tenement courts—in which a large proportion of the inoculations had been made. I was assisted in this investigation by Dr. R. Cleary, an American physician, who has resided for many years in Brazil, and has recently located in Rio for the practice of his profession. Dr. Cleary's assistance, rendered without compensation, was extremely valuable to me on account of his knowledge of the Portuguese language and of the habits and characters of the lower classes of the population among whom the inoculations had been made. I take this occasion to thank him for his kind assistance.

I also employed for six weeks a gentleman of American birth, who is now a citizen of Brazil, to assist me in making these researches, and in translating from the Portuguese articles from the newspapers and from the printed proceedings of the Imperial Academy of Medicine, relating to Dr. Freire's inoculations. Mr. Slaughter, the gentleman referred to, visited the address of a considerable number of the persons inoculated in 1884, for the purpose of ascertaining whether an attack of yellow fever had since occurred. The general results of his researches are given in my report.

As I have already stated, Dr. Freire has failed to convince any considerable number of his medical confrères of the veritable nature of his discovery, or of the value of his protective inoculations, and his work has received very severe, and as I think just, criticism at the hands of some of the members of the Imperial Academy of Medicine. On the other hand he has some ardent admirers among his colleagues of the faculty of medicine and the students who have attended his lectures as professor of organic and biologic chemistry.

Among the laity there are, as might be expected, a variety of opinions. Persons unaccustomed to scientific methods are very liable to form positive opinions upon very imperfect evidence. Thus one intelligent gentleman told me that he had a great deal of faith in Dr. Freire's inoculations, for his barber had been inoculated, and had

not contracted yellow fever. Yet this gentleman was perfectly aware that there are thousands of foreigners—English, Germans, French, Portuguese, and Americans—in Rio who have passed through one or more epidemics of yellow fever without contracting the disease, and who have not been inoculated. Another intelligent merchant gave as evidence of the success of Dr. Freire's inoculations the case of a Portuguese family recently arrived in Brazil, consisting of three members, a man, his wife, and his wife's mother. The two women were inoculated by Dr. Freire; the man was not. All three were taken sick during the epidemic season; the man died, and the two women recovered after a very severe attack of the disease. Instead of giving evidence of the protective value of the inoculation practiced, as my informant was disposed to believe, this case seems to me to prove the contrary, for the two women suffered severe attacks of the disease. The circumstance that they did not die while the man attacked at the same time did is not at all remarkable or unusual, and there is no reason for ascribing it to the fact that they had been previously inoculated.

Beside this case we may put that of the family referred to in a communication from the Baron de Ibituruna, president of the central board of health: "There have already been recorded many deaths among persons inoculated with the 'microbian liquid,' including a respectable family vaccinated a year ago in Catumby. One member of this family died of a pernicious lymphatitis a few days after vaccination, and another of yellow fever a little over two months ago. Every one else in the house had yellow fever, although vaccinated. The person who fared best, having only a mild attack, was one who was absent when Dr. Freire invaded the house and performed the vaccinations without the previous consent of the head of the family."

Again, as showing the kind of evidence which satisfies some minds, I may refer to the case of an American physician and missionary residing in San Paolo. This gentleman came to Rio during the prevalence of yellow fever in 1886, *en route* to the United States. He was inoculated by Dr. Freire, and published his case as evidence of the protective value of such inoculations. But I am informed by no less an authority than our minister to Brazil that this gentleman sailed for the United States a short time after the inoculation was practiced, and that he spent the intervening time at Petropolis, where yellow fever never prevails. Moreover, I am informed from another source that the gentleman referred to was some years ago engaged in business in the city of Rio, and resided in that city for several years. What protected him from contracting yellow fever at that time? Or, if he had the disease then, what value can be attached to the fact that he did not have it after being inoculated? Again, I may point to the fact that many foreigners, including the American consul, passed through the entire epidemic season of 1866, remaining in the city of Rio, without contracting the disease, although they had not been inoculated.

I desire to express here my thanks to Dr. Nuno d'Andrada, director of ports, and to Dr. L. M. Pinto Netto, director of the Jurujuba Hospital, for their kindness in giving me an opportunity to visit the yellow-fever hospital, and for a transcript of the mortality lists for the years 1884, 1885, 1886, and 1887. I am also indebted to Dr. Carlos Frederic, medical inspector-general of the army, for his courtesy in showing me the admirable military hospital under his direction, which is located upon an island in the bay of Rio.

I sailed from Rio on the 11th of August with the intention of taking a steamer at Barbadoes or at St. Thomas, if I should find one in either of these ports which would take me to Vera Cruz or to some port in direct communication with that city. But owing to the prevalence of small-pox in Brazil no passengers were permitted to land from our steamer at the ports mentioned, and I had no choice but to go on to New York.

From New York I proceeded by rail to the city of Mexico, for the purpose of making the acquaintance of Dr. Carmona y Valle, and of investigating his method of inoculation. My orders required me to complete my investigation by the first of October,

but it was evident that the time remaining was insufficient to enable me to comply in a satisfactory manner with that portion of my instructions relating to "the method of inoculation practiced by Dr. Carmona y Valle." I therefore addressed the following letter to the honorable Secretary of the Treasury on the day of my departure:

BALTIMORE, *September* 6, 1887.

SIR: I have the honor to report my departure this day for Mexico, in compliance with special instructions signed by the President.

As explained in my letter of September 4, I was unable to proceed to Mexico by way of Barbadoes or St. Thomas on account of the quarantine at those ports, which prevented any passengers from Brazil from landing. My shortest practicable route was therefore by way of New York.

I would respectfully request that the time fixed for the investigation with which I am charged may be extended for twenty days. It will be about the middle of September before I can reach Vera Cruz, and if I am required to return to Washington by the 1st of October, in compliance with my present orders, it is evident that I can not make an investigation that would be creditable to myself or to the Government.

I shall collect pathological material in Mexico for study in my laboratory during the winter, and it is my desire to make certain researches and experiments after my return to Baltimore, which seem to me to be essential in order to clear up some unsettled questions in connection with the subject of protective inoculations against yellow fever.

So far as I can judge at present this work will occupy me for about four months, at the expiration of which time I will be prepared to make a detailed report of the results of my investigations.

If the twenty days additional time which I consider necessary in Mexico is granted, I would respectfully request that I may be so informed by letter or telegram addressed to me in care of the United States minister in Mexico.

Very respectfully,

GEO. M. STERNBERG,
Surgeon, U. S. Army.

The SECRETARY OF THE TREASURY.

In reply to this communication, I received the following:

TREASURY DEPARTMENT,
Washington, September 17, 1887.

SIR: Referring to the special instructions given you at the time of your detail to conduct the investigation relative to the method of inoculation for the prevention of yellow fever as practiced in Brazil and Mexico, you are hereby granted twenty days' additional time for the conduct of the investigation, as requested in your letter of September 6.

By direction of the President.

Respectfully yours,

HUGH S. THOMPSON,
Acting Secretary.

Maj. GEORGE M. STERNBERG,
Surgeon U. S. Army, City of Mexico, Mexico.

Immediately upon my arrival in the City of Mexico I presented my credentials to the United States minister, Judge Maynard, who received me very kindly, and the following day presented me to Mr. Marascal, secretary of foreign affairs, and to General Diaz, President of the Mexican Republic. From these gentlemen I received assurances that the Government would do all in its power to further the object of my mission, and the following day Mr. Marascal was kind enough to send me a letter to Prof. Carmona y Valle, who is director of the faculty of the national medical college of Mexico, and another to the governor of the State of Vera Cruz, through whom I would be able to obtain the facilities required in the prosecution of my investigations in the city of Vera Cruz.

Prof. Carmona y Valle received me with great courtesy and at once made an appointment with me to visit his laboratory, which is favorably located at the very top of the medical college building. At the laboratory I met his principal assistant, now professor of bacteriology in the medical faculty, Dr. Angel Gavino Yglesias. I was much pleased with the laboratory, which is kept in perfect order and is well equipped with

all the apparatus required for bacteriological researches. It contained a complete set of Koch's apparatus, apparently a recent acquisition, two of Zeiss's largest microscopes, and a full series of objectives by the same maker; also a large English binocular microscope. Prof. Carmona y Valle exhibited to me cultures of his yellow-fever microbe, and mounted preparations of the same, stained with the different aniline colors; also well-made sections of the liver and kidney, stained in hæmotoxylin and in picro-carmine. These preparations were the work of Dr. Gavino, and I take pleasure in complimenting this gentleman upon his technic. I regret to say that I can not accept Dr. Carmona's conclusions with reference to the origin and etiological role of the micro-organisms which he presented to me as coming from the blood and from the urine of yellow-fever patients. I think I will be able to prove to him in my detailed report that they are altogether accidental and without significance so far as this disease is concerned; that the blood and tissues of yellow-fever patients do not contain organisms such as he exhibited to me in his cultures; that these cultures contain a micrococcus and a bacillus, which are specifically different and bear no relation the one to the other, except the accidental one of being associated in his cultures; that therefore his inference that the spherical organisms—micrococci—are "zoospores" which may develop into bacilli, and that these again break up into spherical organisms is a mistake; that the movements of these "zoospores" observed by him and exhibited to me, which he says are not arrested by a temperature of 160° C., or by forty-eight hours' exposure to a 1 per cent. solution of mercuric chloride, are molecular and not vital movements; that the dark-colored granules in his sections of kidney and liver, stained with picro-carmine and hæmotoxylin, do not correspond with the organisms contained in his cultures, and in fact are not micro-organisms. While differing radically with the learned professor in all of these particulars, I desire to testify my high appreciation of his laudable effort to apply scientific methods to the study of yellow fever. If he had been situated more favorably for the study of this disease I dare say he would have found out for himself the source of the errors into which I believe he has fallen; but having to depend upon others to collect his material at a distant locality his misfortune has been that the specimens of urine and blood which have served to start his cultures contained extraneous organisms, which bear no relation to the disease he had undertaken to study.

At Vera Cruz, the principal Mexican sea-port on the Gulf, yellow fever has been endemic for many years, but at the capital and other cities of the interior in an elevated situation the disease is unknown except for the occasional cases which occur among those who have recently been exposed in the infected sea-port.

No extension of the disease occurs from such cases, and this is in conformity with what has been constantly observed elsewhere, as, for example, at Petropolis, the summer residence of the Emperor of Brazil, and the principal health resort of the court and of the foreign residents of Rio de Janeiro during the summer months. This place is located in the mountains at an elevation of 3,000 feet and is only a few hours distant from the city. It is quite a frequent occurrence for those who seek this place of safety during the epidemic season to go to the city during the day, returning to Petropolis in the evening, and not infrequently such persons fall sick with yellow fever and die; but they do not establish a new center of infection in Petropolis or communicate the disease to those in immediate attendance upon them.

The inoculations practiced by Dr. Carmona y Valle had for the most part been made in Vera Cruz, and this was the place [illegible] I hoped to have an opportunity to make some personal observations and experiments relating to the investigation with which I was charged. I proceeded, therefore, as soon as possible to this city. At my request, and by permission of the president of the faculty of medicine (Dr. Carmona), I was accompanied by Dr. Gavino, who took with him the necessary microscopical apparatus to enable him to assist me in my researches. Upon our arrival we established a laboratory in our rooms upon the upper floor of the Hotel de Mexico, and hastened to put ourselves in communication with the physicians in charge of the civil and the military hospitals, who placed their wards at our service and did everything in

their power to further the object of my mission. I am especially indebted to Dr. Daniel Ruiz, director of the civil hospital, for most valuable assistance in my experimental researches. Unfortunately for my object there were but few typical cases of yellow fever in Vera Cruz during the time I was able to remain there (three weeks), and I was not able to secure an autopsy in a single undoubted case. I had supposed that there would be no difficulty in obtaining all the autopsies I desired at this season of the year—the last of September and first October—but the whole summer has been characterized by a remarkable exemption from the disease, and the few cases which I found in the hospitals were of a comparatively mild type and ended in recovery.

The following table shows the mortality from yellow fever in the city of Vera Cruz for each month from January, 1867, to December, 1881. The table is copied from the thesis of Dr. Zacarias R. Molina, a medical officer of the army, who has been for a number of years on duty at the military hospital in Vera Cruz, and who is at the present time also director of the hospital for women:

MORTALITY FROM YELLOW FEVER IN THE CITY OF VERA CRUZ.

Month.	1867.	1868.	1869.	1870.	1871.	1872.	1873.	1874.	1875.	1876.	1877.	1878.	1879.	1880.	1881.
January	.....	7	.....	.....	3	2	1	1	7	.....	.....	16	6	2	28
February	.....	6	.....	.....	.....	2	.....	2	2	1	1	5	4	. .	22
March	.....	7	.....	.....	1	4	.....	.....	4	1	.....	..	2	1	29
April	.....	31	2	.....	6	5	3	.....	11	.....	...	1	1	1	29
May	.....	42	.....	.....	19	14	1	2	25	.....	4	7	1	.....	94
June	.....	16	.....	.....	113	45	19	3	93	2	7	58	1	...	233
July	8	28	1	.....	71	53	59	11	118	4	54	114	2	1	132
August	29	21	1	... .	17	39	59	24	105	7	144	110	1	3	39
September	36	21	.....	.....	10	29	44	7	41	9	164	62	3	9	22
October	17	9	1	3	15	11	20	12	13	6	77	45	.....	42	25
November	11	2	2	5	2	..	10	11	2	1	50	24	.....	92	18
December	8	3	.....	2	4	6	7	6	.....	3	27	7	.....	98	4
Total	109	193	7	10	271	210	223	79	425	34	528	444	21	249	675

I have not obtained the total mortality for the city from the year 1881 to date, but the following table, giving the number of deaths in the civil hospital from January, 1882, to December, 1886, will serve as an index of the prevalence of the disease during this period:

DEATHS FROM YELLOW FEVER IN THE HOSPITAL OF SAN SEBASTIAN, VERA CRUZ.

Month.	1882.	1883.	1884.	1885.	1886.	Month.	1882.	1883.	1884.	1885.	1886.
January	.....	4	.....	.....	.....	August	6	7	2	29	11
February	1	2	.....	.....	.....	September	2	16	5	10	6
March	1	5	.....	.....	.....	October	2	15	2	4	5
April	.....	7	.....	.....	.....	November	2	6	3	2	.....
May	.....	39	1	1	.....	December	4	3	2	2	.....
June	2	126	.....	6	1						
July	2	83	2	36	2	Total	22	313	17	90	25

A glance at these tables shows that the season of greatest prevalence is from May to October, but that cases occur during every month of the year; further, that certain years, *e. g.*, 1875, 1877, 1881, are characterized by a very considerable mortality, and may be designated epidemic years, while in other years, *e. g.*, 1869, 1870, 1879, the mortality is comparatively small. The fact that the disease in question is endemic at Vera Cruz is very clearly brought out by these tables, and yet it is evident that the conditions which govern its prevalence are variable, for in certain years the season of greatest prevalence has passed without being marked by an increase in the number of cases, as in 1879 and 1880; and sometimes after a comparatively healthy

summer, an epidemic of moderate proportions has been developed during the autumn months, as in 1880.

Dr. Molina accounts for these fluctuations by differences in the meteorological conditions, and especially in the temperature and prevailing winds, two meteorological factors which at Vera Cruz are closely allied. No doubt these are important elements in accounting for the notable differences in the mortality during different years; but there are other factors to be taken into consideration, and especially the number of susceptible strangers present in the infected area during the periods to which the figures relate. The following table which we also copy from the thesis of Dr. Molina shows in parallel columns the temperature, the direction of the prevailing wind, and the mortality from yellow fever during the years 1878, 1879, 1880, and 1881:

MORTALITY FROM YELLOW FEVER, MONTHLY MEAN TEMPERATURE, AND PREVAILING WINDS, CITY OF VERA CRUZ.

Month.	1878.				1879.			
	Temperature.		Winds.	Deaths.	Temperature.		Winds.	Deaths.
	C.	Fahr.			C.	Fahr.		
	°	°			°	°		
January	20.87	69.5	NW.–N.	16	22.76	72.9	NW.–SE.	6
February	22.22	72	N.–NW.	5	22.65	72.8	NW.–N.	4
March	24.30	76	SE.–NW.	.....	25.61	78.9	NW.–SE.	2
April	26.89	80.5	NW.–SE.	1	26.16	79	SE.–NW.	1
May	29 04	84.3	SE.–NE.	7	28.59	83.4	SE.–NW.	1
June	30.49	86.9	SE.–NE.	58	28.67	83.5	NW.–SE.	1
July	29.78	85.6	SE.–NW.	114	29.80	85.6	SE.–NW.	2
August	29.23	84.6	SE.–NW.	110	30.31	86.5	NW.–SE	1
September	28.57	83.4	NW.–SE.	62	27.08	80.7	NW.–N.	3
October	27.33	81.2	NW.–SE.	45	26.14	79	NW.–N.	.....
November	25.15	77.3	NW.–SE.	24	26.02	79	NW.–SE.	.....
December	21.26	70.2	NW.–N.	7	23.05	73.4	NW.–N.	.....

Month.	1880.				1881.			
	Temperature.		Winds.	Deaths.	Temperature.		Winds.	Deaths.
	C.	Fahr.			C.	Fahr.		
	°	°			°	°		
January	23.03	73.2	NW.–SE.	2	19.33	67.3	N.–NW.	28
February	24.08	75.3	N.–SE.	6	19.68	67.4	N.–SE.	22
March	25.60	78.1	SE.–NW.	1	24.15	75.4	SE.–N.	29
April	27.15	80.8	SE.–NW.	1	25.05	77.1	SE.–N.	29
May	29.40	84.9	SE.–NW.	.....	28.05	82.5	SE.–S.	94
June	30.25	86.4	SE.–NW.	.....	29.20	84.6	SE.–S.	233
July	30.92	87.6	SE.–NW.	1	31.15	88.1	SE.–S.	132
August	30.10	86.2	SE.–NW.	3	30.92	87.6	SE.–NW.	39
September	28.50	83.3	NW.–SE.	9	29.06	84.3	SE.–NW.	22
October	25.30	77.5	N.–NW.	42	27.01	80.6	N.–NW.	25
November	24.87	76.7	N.–NW.	92	24.05	75.3	N.–NW.	18
December	23.73	74.7	N.–SE.	98	23.15	73.6	N.–NW.	4

An inspection of the above table shows that northerly winds prevail during the autumn and winter months, and that during the summer easterly and southerly winds are more prevalent. We note that during the months of May, June, and July, 1881, during which yellow fever prevailed as an epidemic, with a mortality for the three months of 459, the wind was constantly from the south and southeast, while during the preceding year it was during the same period from the southeast and northwest, and the mortality was but one. Such a comparison, however, has no great value, for we find that in the same year 1880, after an unusually healthy summer yellow fever

prevailed to a considerable extent during the months of September, October, November, and December, with prevailing winds from the north and northwest, and a temperature lower than during the corresponding months of the preceding year (1879), when there was no yellow fever. Again, we see that this epidemic influence which showed itself in the fall of 1880 manifested itself throughout the whole of the following year. We note, too, that the temperature during the four months of greatest epidemic prevalence in 1881 was lower in two (April and May) and only slightly higher in two (June and July) than during the corresponding months of the preceding year. It is evident, therefore, that other factors must be sought in order to account for the unusual prevalence of the disease during certain years. The general fact shown by the table and by observation, can not, however, be disputed, viz, that the greatest mortality is during the months with the highest mean temperature, and that the prevalence of northerly winds has a tendency to put an end to the epidemic extension of the disease.

The physicians attending the civil and military hospitals in Vera Cruz were, of course, familiar with the claims of Dr. Carmona to have discovered the germ of yellow fever and a method of protective inoculation, but I could not learn that any of them had confidence in the method, which had been extensively tested in Vera Cruz in the year 1885 under their immediate observation. On the contrary, facts were mentioned to me which were directly opposed to an acceptance of the view that the inoculations practiced exercised a protective influence. I shall discuss the evidence relating to this subject in the body of my report, but may remark here that so far as I could learn the results obtained in 1885 were not sufficiently encouraging to induce any one to continue the practice in Vera Cruz, and I believe that Dr. Carmona himself has not made any considerable number of inoculations since the date mentioned. As already stated I found a few non-fatal cases of yellow fever in the hospitals of Vera Cruz, but very much to my disappointment did not have an opportunity to make an autopsy in a single fatal case.* It had been my special desire to inoculate various culture-media with blood from the heart and with material from the liver, kidneys, etc., for the purpose of ascertaining whether any micro-organisms would develop from such material; and also to make cultures from the contents of the stomach, the intestine, and the bladder by puncturing their walls, and thus withdrawing the material through a capillary tube without any danger of external contamination. Such experiments to have value should be made at the earliest possible moment after death. But notwithstanding my desires and best efforts I was obliged to return at the expiration of the time fixed by my orders, and the extension of twenty days for which I had asked, without having made these very important experiments, which possibly might throw light upon the etiological problem which has so earnestly engaged my attention.

I had previously attempted to solve the question as to the presence of micro-organisms in the blood and tissues by direct examination of blood drawn from the finger, in Havana in 1879, and in Rio during my recent visit to that city, and by examining thin sections, stained by various methods, of liver, kidney, and stomach from typical cases of yellow fever. The result of these researches had been negative, but it is possible that by culture-experiments an organism might be discovered that has escaped observation by these methods of investigation. I shall therefore consider my work incomplete in this particular so long as I have not had an opportunity to make inoculations, in suitable sterilized culture-media, with material taken from the organs which show the principal pathological changes in this disease—the liver and kidneys.*

In anticipation of the possibility that I might fail to secure autopsies in Vera Cruz as I had done in Rio, before leaving the last-mentioned city, I wrote to my friend Dr.

*I have since had ample opportunity to make the researches referred to, having made ten autopsies in typical yellow fever cases in Havana in the summer of 1888, and thirty during the summer of 1889.

Daniel M. Burgess, of the Marine-Hospital Service, an American physician, who has been practicing medicine for many years in Havana, requesting him to secure pathological material for me from a number of typical cases of yellow fever. Dr. Burgess had previously sent me such material (in 1885), from two cases, and I had made and stained, by various methods, a large number of sections. But I desired to continue this research and accordingly wrote for more material, with the condition that it must be obtained and put in strong alcohol as soon as possible after the death of the patient. Soon after my return to Baltimore I received from Dr. Burgess material from four typical cases, and later from another. Before leaving Rio I had also received from my friend, Dr. Aranjo Góes, material from nine cases, which he had preserved in aclohol since the year 1884. The careful study of this material and of the cultures brought back with me from the laboratories of Dr. Freire and Dr. Carmona has occupied a large portion of my time since my return from Mexico. I have also had an opportunity during the past winter to study some cultures made in Havana by Dr. Carlos Finlay, by whom they were sent to Prof. William Welch, M. D., of the Johns Hopkins University. Dr. Welch kindly placed these cultures in my hands and I shall give a detailed account of the result of my examination of them in the body of my report. I desire here to express my thanks to Professor Welch, in whose laboratory my researches have been made, for numerous favors, and for valuable suggestions with reference to the prosecution of my work.

REPORT ON THE CRYPTOCOCCUS XANTHOGENICUS OF DR. DOMINGOS FREIRE.

The claims of Dr. Domingos Freire, of Brazil, to have discovered the specific cause of yellow fever and a method of preventing the disease by inoculation with an "attenuated virus" are contained in the following published works:

1. Recherches sur la cause, la nature et le traitement de la fièvre jaune, Rio, 1880.
2. Études expérimentales sur la contagion de la fièvre jaune, Rio, 1884.
3. Mémoire sur les ptomaïnes de la fièvre jaune, Rio, 1885.
4. Doctrine microbienne de la fièvre jaune, et ses inoculations préventives; un gros volume de 630 pages. Rio, 1885.

Le vaccin de la fièvre jaune. Résultats statistiques des inoculations préventives pratiquées avec la culture du microbe atténué, de janvier à août de 1885, Rio, 1885.

5. Considérations sur le vaccin de la fièvre jaune (Publiées dans la Revue des cours pratiques et théoriques de la Faculté de Médecine de Rio de Janeiro). Rio, 1886.
6. Notice sur la régénération de la virulence des cultures atténuées du microbe de la fièvre jaune. Rio, 1886.
7. Conférence sur le microbe de la fièvre jaune, prononcée devant la Société de thérapeutique dosimétrique de Paris, et publiée dans le Répertoire universel de la même Société, numéro de mai 1887, Paris.
8. Du microbe de la fièvre jaune et de son atténuation, note présentée à l'Académie des Sciences (en collaboration avec MM. Paul Gibier et C. Rebourgeon), Paris, 1887.
9. Résultats obtenus par l'inoculation préventive du virus atténué de la fièvre jaune (*Idem*), 1887, Paris.

Dr. Freire's principal work, "Doctrine Microbienne de la fièvre jaune," was published in 1885, at the expense of the Brazilian Government, at a time when he enjoyed the confidence of the minister, and was president of the Junte Centrale d'Hygiène Publique. It is illustrated with numerous chromo-lithographic plates, and with sphygmographic tracings, temperature charts, etc.

Dr. Freire's instructions from the minister of the Empire are given in the introduction to this work, as follows:

OFFICE OF THE MINISTER OF THE EMPIRE,
Rio de Janeiro, March 15, 1883.

The Government having decided to give the greatest attention to the study, and to a knowledge of the cause and treatment of the various diseases which attack this city with the greatest intensity, charges you to continue the studies which you commenced in 1880 upon the cause, the nature, and the treatment of yellow fever. You should keep in view that the studies which you make include:

(1) Microscopic observations and cultures of the microbes encountered in the humors.

(2) The attenuation of the virulence of the same microbes, and experiments in the vaccination of animals for the purpose of ascertaining if it is possible to employ these microbes as a means of prophylaxis.

(3) The employment of salicylate of soda as a mode of treatment, by the stomach and hypodermatically.

(4) Autopsies, and the determination of the anatomico-pathological lesions produced by the morbid process.

I authorize you to name three students, who will each receive a monthly salary of 120$000 ($55), to aid you in these studies, which will be made in the maritime hospital of Santa Isabel, in an infirmary which will be designated by the inspector of health, to whom I have this day communicated this resolution.

The Government attaches the greatest importance to your studies, which if they are crowned with a happy result, will merit a recompense proportioned to the services which you shall have rendered.

May God protect you,

PEDRO LEÃO VELLOSO.

In the introduction to his work referred to Dr. Freire claims priority of discovery and confirmation from independent sources in the following language:

"As the question of priority of discovery of the parasite of yellow fever has been agitated, the reader will pardon me if I give here the reasons which favor the right which I consider belongs to me. A year after I had announced my discovery M. Carmona y Valle, professor in the University of Mexico, observing under the microscope different specimens of urine brought from Vera Cruz and coming from patients with yellow fever, found likewise in this liquid the cellular elements, which by the description which he has made of them may be recognized as identical with those which I had so minutely described. * * * . Some differences have arisen with reference to the classification and the development; but I hope that after reading the descriptions which I shall make further on all doubt will cease, for it will be seen that I have cultivated the parasite with all precautions, all the technical rigor possible; that I have been able to follow its evolution and to characterize it as an alga, a cryptococcus and not a fungus, as M. Carmona thinks, who has not proceeded to employ Pasteur's method of cultivation as I have done.

"Besides, I have also in my favor the observations of Granizo y Ramirez, the author of an important treatise upon yellow fever published this year. This author writes me, 'Your observations have been verified here, not only by myself, but by several of my military colleagues.'

"Dr. Joseph Jones, also, in observing the constitution of the atmosphere during an epidemic of yellow fever in New Orleans, expresses himself as follows in his report to the board of health of Louisiana, published in 1883:

"'In this way I have submitted to a microscopical and chemical examination the air of localities and apartments infected with the germ of yellow fever, and I have distinguished a great number of living organic particles, very small, and which might be called spores, having a diameter of one ten-thousandth to one three-thousandth of an inch, also a large number of living animalculæ, together with particles of fatty substances, fibers of clothing, and from the bed linen. The spores resembled very much *micrococci* and the *cryptococci* of Hallier. I have observed similar particles in the blood of yellow-fever patients and I have observed bacteria in the air and in the blood.'

"These *cryptococci* which Jones found in 1883 in the air and in the blood are not different from those which I have isolated and described in 1880, those which I have proved to be the living factors in the evolution of yellow fever.

"It is true that M. Babes, analyzing (we think with little care) some fragments of viscera which had been sent him by some one in Brazil, I do not know in what condition, in flasks not suitably prepared and in alcohol full of organic dust, has concluded without any further preamble that my observations were badly made. * * * M. Babes has surely been the unconscious victim of some scientific treason. * * * When one has before his eyes the excellent result of the preventive inoculations made, which will be found at the end of the present work, it will be necessary for him to submit to the evidence of facts. * * * I consider, then, this problem of the preventive inoculation of yellow fever, the final end of all my researches, to be entirely resolved."

In the first chapter of Dr. Freire's work at present under consideration the morphology of his *Cryptococcus xanthogenicus* and its mode of development are again given, in accordance with his previous descriptions, as follows:

"When we follow, with all the care and attention possible, the march of the development which characterizes the germs which produce yellow fever, we acquire the certainty that, commencing to present themselves under the form of little points almost imperceptible, they afterwards gradually increase in diameter until they attain considerable dimensions; so that these little beings, which at the outset had the aspect of very little grains of sand, not measuring more than 0.001^{mm} to 0.002^{mm} in diameter, arrive, little by little, to such a development that they reach the dimensions

of 0.005, 0.007, or 0.008mm, and sometimes even more in certain determined conditions.

"When they have attained the adult age these cells are broken at diverse points and discharge their contents, composed of spores already formed, mixed with a viscous substance of a yellow color, composed of a pigmentary and protoplasmic substance, and of the liquids elaborated by the cells. * * *

"The *microbe xanthogenicus* is a cosmopolitan; it does not select its domicile in any organ and has no preference for any organic liquid. We have encountered it with the same characters, the same opulence of proliferation, in the brain, in the muscles, in the liver, in the spleen, in the kidneys, in the lungs, in the blood, in the urine, in the bile, in the vomit, and even in the cephalo-rachidian fluid. However, it is necessary to establish a well-drawn distinction as to the blood. The blood of the general circulation shows itself much less charged with the microbes than the blood of the capillaries. Thus, if I could admit any preference on the part of the *microbe xanthogenicus*, I would say that it pleases itself better in the blood of the capillaries, in the blood which bathes immediately the anatomical elements. * * *

"The occasion seems to us a favorable one in order to call attention to some indispensable precautions when the microbes of yellow fever are to be sought in organic solids and liquids. While it is extremely easy to perceive the presence of the microbes of yellow fever in the urine and the bile, for example, by placing a drop of these liquids upon a glass slide, covering it with a thin glass cover, and examining it with a power of 450 to 740 or 780 diameters, this proceeding can not be employed when the blood is to be examined. If we proceed in this manner the globules will hide nearly all of the microbes, and the observer will wrongly conclude that they are very rare in this organic liquid. Not only does the form of the microbe offer a certain resemblance to that of the red corpuscles, but these latter in adhering together envelope the microbian cells, and, on the other hand, cast upon the cells a jet of light which makes them disappear from the field of the microscope. But if we dilute a little drop of blood in a pure solution of sulphate of soda and place it under the objective, the microbes become visible and will appear in considerable quantity.

"It is likewise necessary to make a preparation previously for the examination of the cerebal mass and of the muscles. They should be triturated in a sterilized mortar and mixed afterward with distilled water entirely deprived of organisms, filtred through fine linen which has been passed rapidly through the flame of an alcohol lamp, and afterwards a drop of the filtered liquid should be placed upon a glass slide. If we withdraw a little piece of brain or of muscular fiber, even triturated, we will not perceive anything abnormal under the microscope unless it be the anatomical elements more or less deformed by trituration.

"It is not the same for the liver. It suffices to withdraw a bit of this organ and to crush it between two glass slides; upon observing it under the microscope we perceive at once a multitude of microbes. This is because in the muscles the microbes are lodged between the fibrillæ and in the substance which surrounds them; and in the brain they are found in the interior of the nerve-cells, which must first be destroyed by trituration in order that their parasitic hosts may become visible."

I would say in the first place that the description above given of the *cryptococcus xanthogenicus* does not correspond with the characters of the micro-organism which Dr. Freire presented to me as his yellow-fever germ; and, secondly, that no such organism as he has described, or as was present in the cultures which he gave me, is to be found in the blood or tissues of yellow-fever patients.

The remarkable account of the morphology of his cryptococcus, which Dr. Freire has given on different pages of his principal work, has been pointed out by one of his medical confréres in Rio, in the following language:

In the second part of the order of the day the subject discussed was the etiology of yellow fever. After a brief exordium, Dr. Aranjo Góes said that there are two parasites which are presented as factors of the yellow fever, the *cryptococcus xanthogenicus* of Dr. Freire and the *peronospora lutea* of Dr. Carmona, of Mexico.

He wished in the first place to make the Academy acquainted with the *Cryptococcus xanthogenicus*. It is an alga to which has been given the specific title of *xanthogenic*. As to its appearance, he would quote Dr. Freire's own description, which is as follows: Page 11 of his work: Round, green cells, with a black border. Page 12: Round and gray, with a black ring, large and small. Page 12: Large, black, round corpuseles, brown cells. Page 13: Black or gray corpuscles. Page 13: Corpuseles of the size of grains of sand, or pin-heads, larger gray organisms with *green and red* tints, *others with a dark or black border*, and with bright spots in the center vividly reflecting the light. Page 14: Spherical corpuscles, with black borders. Page 15: Cells of considerable size, somewhat elongated or ellipsoid, with granulations. Page 25: Small black points, round cells, brown or black, vividly reflecting the light, irridescent, granular, with yellow and *green* pigments. Page 26: Ovoid or eliptical. Page 39: Green with dark borders, black. Page 40: Series of very fine black points; other spots larger and surrounded with dark borders; others still larger, of a greenish appearance, with changeable tints; others large, encircled in a dark belt with a bright spot in the center. Page 42: Large green cells with changeable tints; others very small and bright in the center, encircled in a dark belt. Page 43: Round corpuscles resembling small grains; others larger with a bright spot in the center. Page 44: Black borders encircling a bright spot; others resembling a bunch of grapes. Page 77, a rosary of round corpuscles with green tints. Page 81: Cryptococci red in the center, with a green border, others brown. Page 84: Green, with changeable tints and with the shape of a triangular pyramid. Page 85: Long mycellia with ramified spores. Page 86: Pyramidical bodies, bright and yellow. Page 79: Black corpuscles, others larger and brown, many of them with bright red borders, there being one conspicuous for its beauty, a red pyriform corpuscle with green borders. Page 226: Black spots, roundish corpuseles vividly reflecting the light, either brown or black or with black borders. Going back to 1883 (*Études Expérimentales sur la Contagion de la Fièvre Jaune*), we see that the *cryptococcus* is elongated and ramified, like the mushroom on being brought into contact with air, or like the *bacteria* of the carbuncle or the *mycoderma cerevisiæ*. Preface JJ, page 2: Transparent granulations inclosed in a covering containing yellow pigment. Page 12: Black granulations. Going back still farther, to the year 1880 (*Travaux Chimiques*), we see new forms. Page 225: Smoke-colored cells. Page 228: *Cryptococci* of variable sizes, some enormous with a bright space in the center, gray with a dark yellow segment, angular with an irregular polyhedric shape, fringed, without bright spots or segmental penumbra. Page 231: Granular *cryptococci* (*antheridiæ* and *sporangi*). This multiplicity of forms indicates that Dr. Friere has taken for *cryptococci* blood and fat globules and various mucid productions (mildew).

* * * * * * *

The speaker compared two more extracts from Dr. Freire's works with paragraphs in the "Archives of Physiology," showing that the *cryptococcus xanthogenicus* and the transformed blood globules and hæmatoblasts are perfectly alike.

In answer to a remark relating to the difference between microbes and the elements of the blood in regard to the power of motion, the speaker said that the capillary currents between two glass plates produce a perfect imitation of animated motion.

"In order to observe the microbes in the muscles, nervous centers and kidneys," says Dr. Freire, it is necessary to "examine with the microscope distilled water in which these organs have been triturated. In this way, and in this way only, myriads of microbes may be seen. In no other way would it be possible to discover them, for the microgerms are inclosed in the sarcolema of the muscular fibers, in the nerve cells, and in I know not what element of the kidneys."

Making some reflections on this, the speaker observed that, if the shreds of the fibrillæ may be distinctly seen through the sarcolema, still more plainly visible should be the *cryptococci* which attain large proportions—eight thousandths of a millimeter, and even ten times larger, as is stated by the author of the Etiology of Yellow Fever.

If Dr. Freire could not see the microbe through the transparent sarcolema and nerve cells, it is because it was not there to be seen. If, after triturating the viscera he saw it, it is because the trituration separated the fat globules, and he took these for *cryptococci*. And so indisputable is this that Dr. Freire, referring to the liver, says: "Here we dispense with the preliminary process of trituration; it suffices to place a piece of liver between two plates and press them together, and innumerable microbes will be seen." (Page 6.)

Indeed, such must necessarily be the case, for the fatty degeneration of the hepatic gland furnishes a large quantity of fat globules without any necessity for triturating the tissues. The speaker added that what he had said on this subject was not mere theory, but the result of experiments made during three years. Tens of times he had seen the fat globules of the liver which are classified as microbes by Dr. Freire. A little ether or osmic acid would suffice to settle the question.

If Dr. Freire wished to show that micro-organisms were to be found in the viscera,

he should make use of the *only* scientific method of doing this. He should make histological sections, and thus he could indisputably prove the existence of his *cryptococcus* in the muscles, liver, kidneys, etc.

In his book, however, there is not a single engraving having any reference to this capital point, and this omission is unpardonable.*

It being late, the speaker here terminated his address, promising to continue on the following Tuesday.

The only explanation of this wonderful versatility as to form and color on the part of the "cryptococcus" which I can conceive of is that offered by Dr. Góes, viz: that Dr. Freire has mistaken deformed blood corpuscles, fat globules from the liver, and the débris of tissue elements in his trituration of muscle, brain, etc., for micro-organisms. Indeed, it can scarcely be doubted that such is the case, for, as I shall show later, exact methods of research show that no micro-organisms are present in such material, collected with proper precautions immediately after the death of a yellow-fever patient. Dr. Freire frequently speaks of his cryptococcus as being endowed with active movement. It is well known to microscopists that minute particles, organic or inorganic, when suspended in a fluid, undergo, under certain circumstances, a rapid vibratory motion, known as the brownian or molecular movement. The micro-organism, a micrococcus, which Dr. Freire presented to me as his yellow-fever germ, like other similar organisms, presents these molecular movements when suspended in a fluid, but it has no proper vital movements, such as are manifested by many of the bacilli. The fat drops from crushed liver tissue, or the débris of muscle fibrillæ, present these molecular movements, and in form and appearance present some resemblance to micrococci. They are easily distinguished, however, by chemical tests and staining agents. I may remark here that prior to his visit to Paris in 1887 Dr. Freire seems not to have made use of the method of staining with aniline dyes. In an address, made while in Paris, he defends himself from the charge which some one seems to have made, that he had neglected this means of recognizing micro-organisms, in the following language:

"We know that in order to color a microbe it is necessary, first, to kill it and then to wash the little microscopic cadaver by means of reagents possessing the power of dissolving all matters foreign to its skeleton. At the outset I applied myself to the study of the yellow fever microbe in a fresh state. I fed it with the best food—*les meilleurs engrais*—for the purpose of witnessing the different phases of its evolution from its birth to its death.

"Nevertheless, in fault of other accusations, some authors have reproached me with not having colored my microbe. Alas, what a miserable objection? Is it necessary in order to affirm the existence of a microbe, which swarms by millions in the urine, in the bile, in the blood, in the tissues, etc.—is it necessary to mask them, to disguise them under a costume of carnival, in order to please certain microscopists? M. Pasteur has never colored his microbes; and nevertheless every one admits the existence of the bacillus of charbon, of the corpuscles of pébrine, of the micrococcus of fowl-cholera, etc. * * * Do not think, gentlemen, that I fear the application of coloring processes to the search for the microbe of yellow fever. Far from it. In order to show you that the criticism which I have just made is not due to prejudice, I will say to you that such processes have recently been employed upon the yellow-fever microbe with complete success."*

The method of cultivating in solid media and of isolating micro-organisms by means of plate cultures or Esmarch tubes, seems also to have been unknown to Freire prior to his visit to Paris. All of the cultures left in his laboratory at the time of my arrival were in liquid media and preserved in Pasteur flasks. He brought from Paris, however, a number of cultures in agar-agar, and among them one which he presented to me as a pure culture of his yellow-fever microbe. This was a micrococcus, which

* Dr. Góes, himself, has made numerous histological sections of the organs chiefly involved.

* Répertoire Universel de Médecine Dosimétrique, May, 1887, p. 224.

multiples, as do other micro-organisms of the same class, by binary division, and not by the growth of the separate cells to comparatively large dimensions, and the formation of endogenous spores, which are released by rupture of the cell wall of the mother cell. The latter mode of development is that which Freire has constantly assigned to his *Cryptococcus xanthogenicus*. In his address before the *Dosimétrique* Society of Paris, on the 2d of April, 1887, from which I have already quoted, he says:

"Each adult cell is ruptured in one or several points and allows to escape its contents, composed of germs which are to perpetuate the species and two pigments, one yellow, destined to infiltrate all the tissues and to produce the icteric color which has given name to the malady, the other black, insoluble, and destined to be carried along by the circulatory current, producing either capillary obstructions, or blood stasis in the parenchyma of the organs."

Now this mode of multiplication is not known among the bacteria, and does not occur in the micrococcus which Dr. Freire placed in my hands as his yellow fever microbe. Fig. 1 is carefully drawn from a stained preparation, mounted in the usual manner from an agar-agar culture of this micrococcus, brought by Dr. Freire from Paris. This culture, according to Dr. Freire's statement to me, came originally from the blood of a yellow-fever patient at the point of death.*

FIG. 1.—Micrococcus of Freire. Culture brought from Paris in 1887, and presented to the writer as the microbe of yellow fever. Drawn from a preparation made in Dr. Freire's laboratory. × 1,000.

Dr. Freire's method of obtainining his "cryptococcus" from black vomit is shown by the following quotation from his principal work:

"*Culture from black vomit in bouillon.*—The microbe was sowed on the 28th of March. At the end of five days, that is to say, April 2, we proceeded to examine this culture. There was no putrefactive odor and the liquid was perfectly well preserved. A drop quickly withdrawn showed us under a magnifying power of 740 diameters the following: Numerous black corpuscles; others larger, having the size of a pin's head; others much larger, of a gray color more or less pronounced, endowed with spontaneous movements. In a great many, one perceived a brilliant red border. In the midst of all these cryptococci one was distinguished by its beauty; it was a red corpuscle with a green border, pyriform, which was narrowly attached to an archipelago of granulations; it was a cryptococcus which threw out its contents

* I have had this micrococcus in cultivation ever since my return from Brazil. It is a staphylo coccus which liquifies gelatine rather slowly, and which forms a white mass upon the surface of agar-agar, or of cooked potato. It does not produce black pigment and it is not present in the blood and tissues of yellow-fever cadavers. I have now made cultures from blood obtained from the heart, and material from the liver and kidney, in numerous cases occurring in the wards of the hospitals of Havana during the summer of 1888 and 1889, and I have not in a single instance encountered this micrococcus, or any micro-organism corresponding with Dr. Freire's description of his *Cryptococcus xanthogenicus*.

BALTIMORE, *September* 20, 1889.

of spores and pigment. It is known that in the vomited matter conditions are found favorable for the developement of different germs. It is for this reason that one sees in this culture numerous bacteria, pre-existing in the vomited matter, endowed with movement, in the form of filiments more or less long and slender like ribbons, transparent, isolated or joined in pairs. At this moment one observes four bacteria articulated, forming a single mobile filament, resembling a fragment of chain of a tenia or of a *bothriocephale*. In a great number of points the bacteria were interlaced, forming a vast net-work resembling sometimes fine lace. It is well established that they constitute a matter foreign to the culture of the *Cryptococcus xanthogenicus;* these productions never appear in a pure culture. What is equally interesting is that finally, according as the cryptococcus gains ground, the bacteria have a tendency to disappear, even completely. Indeed, in this same culture, examined five months after, no traces of bacteria were discovered, as may be seen in the accompanying drawing."

This method of obtaining a pure culture is quite a novel one, and judging from the cultures which I examined in Dr. Freire's laboratory, is far from being reliable. Soon after my arrival in Rio, Dr. Freire's assistant, Dr. Chapot Prévost, selected for me a culture from a closet in the laboratory, devoted to the preservation of his yellow-fever cultures. These cultures were all in Pasteur flasks, and the neck of each flask was carefully wound with cotton-wool, to prevent the admission of atmospheric organisms through the ground joint by which access to the flask is obtained. Direct examination of the contents of this flask showed that it contained various organisms, but none resembling the *Cryptococcus xanthogenicus*. I made cultures in agar, in bouillon, and in gelatine from this flask, which was labelled February 13, 1885, and obtained in these cultures a variety of different bacilli, some of which I isolated by means of Esmarch tubes; among these was a small oval bacillus with end staining, resembling somewhat the bacillus of rabbit septicæmia; a slender, straight bacillus with square ends, and a larger bacillus, also with square ends articulated in chains of two or more elements. After Dr. Freire's return (July 14), he placed in my hands another of these flasks dated February 26, 1885, which he said contained a culture originally started from the blood of a fatal case of yellow fever, shortly before death. Direct examination of preparations stained with fuchsin showed that this culture contained at least two species of bacillus, but no micrococci were recognized.

It seems evident from these examinations of Dr. Freire's cultures that his statement that in impure cultures his cryptococcus obtains the mastery over other micro-organisms and remains in possession of the field can scarcely be accepted.

No doubt Dr. Freire has had micrococci in abundance in his cultures made from black vomit, and possibly his cultures from this source may have contained the veritable yellow-fever germ, but it will be conceded by all bacteriologists that by the methods he details it would be quite impossible to demonstrate the fact, if such were the case. As he has said, black vomit contains a variety of micro-organisms, and, as I can affirm from my own observations, among the number there are micrococci of several different species. To demonstrate that any of these is the cause of yellow fever it would be necessary to isolate it in pure cultures, and prove its specific pathogenic power by inoculations in man or in one of the lower animals. This, Dr. Freire has entirely failed to do. As to the cryptococci of various shapes and colors, which he has described in the foregoing quotation from his work, it is evident that his account is founded entirely upon a misinterpretation of what he saw under the microscope. It is the testimony of numerous competent observers that the peculiar color of black vomit is due to the presence of blood which has escaped by passive hemorrhage from the mucous membrane of the stomach. I have verified this fact by microscopic examination, and have in my possession a photo-micrograph, made in Havana

in 1879, which shows it in a most convincing manner. This was made from black vomit, mounted *au naturel*, and shows numerous pale disks, which are evidently decolorized red blood corpuscles, scattered about the field, or agglomerated in little masses. The same photograph shows numerous micrococci and a few bacilli. I have recently examined a large number of stained sections of the stomach from four typical cases of yellow fever, and I find attached to the surface of the mucous membrane various micro-organisms, which I shall describe in detail later. Among these are micrococci, and in some preparations vast numbers of these are massed together upon the surface of the mucous membrane. But these do not correspond either with the *Cryptococcus xanthogenicus*, as described by Dr. Freire, or with the figure which he has given of his culture from black vomit. Whether these micrococci, or any other of the various micro-organisms found in the stomach and intestines of yellow-fever patients are concerned in the etiology of yellow fever, can only be determined by an extended experimental research, in which all of the modern methods for isolating micro-organisms and testing their pathogenic power must be brought into use.

Having demonstrated that the micrococcus presented to me by Dr. Freire as his yellow-fever microbe does not correspond with his descriptions of the *Cryptococcus xanthogenicus*, I shall proceed to make good my second assertion, viz, that *no such organism as he has described, or as was present in the cultures which he gave me, is to be found in the blood or tissues of yellow-fever patients.*

I remark, first, that his micrococcus would be very easy to demonstrate in properly stained preparations of blood or sections of tissues; second, that I have made a multitude of such preparations, but have never encountered it. I would further remark that I have faithfully searched, without any prejudice against the finding of a yellow-fever germ in the blood or tissues, but that on the contrary at the outset of my researches I felt quite sanguine that such a germ would be found when properly looked for. I have long been of the opinion that there must be a micro-organism of some kind concerned in the etiology of yellow fever, and as long ago as 1873 sustained this view in a paper published in the American Journal of the Medical Sciences (April, 1873). Naturally in an infectious disease, in which the liver and kidneys show the most marked pathological changes, we would expect to find the agent which is the cause of the disease, and upon which its infectious nature depends, in the blood or in the parenchyma of the affected organs. Accordingly, I have from the outset of my investigations given special attention to a search for the yellow-fever germ in the blood and tissues of yellow-fever cases.

RESEARCHES BY THE WRITER.

[Extracts from report of Havana commission (1879).]

In Havana Dr. Sternberg gave a large share of his time to the microscopic examination and photography of the blood. No chemical examination was attempted. The patients from whom specimens of blood were obtained were mostly soldiers in the military hospital of San Ambrosio. Ninety-eight specimens from forty-one undoubted cases of yellow fever were carefully studied, and one hundred and five photographic negatives were made, which show satisfactorily everything demonstrable by the microscope. These photographs were mostly made with a magnifying power of 1,450 diameters, obtained by the use of Zeiss's one-eighteenth inch objective and Tolles's amplifier. Probably no better lens than the Zeiss one-eighteenth (oil-immersion) could have been obtained for this work, and it is doubtful whether any objective has ever been made capable of showing more than is revealed by this magnificent lens. With the power used, organisms much smaller than those described as existing in the blood of charbon or of relapsing fever would be clearly defined.

If there is any organism in the blood of yellow fever demonstrable by the highest powers of the microscope as at present perfected, the photo-micrographs taken in Havana should show it. *No such organism is shown in any preparation photographed immediately after collection.* But in certain specimens, kept under observation in culture-cells, hyphomycetous fungi and spherical bacteria made their appearance after an interval of from one to seven days. The appearance of these organisms was, however, exceptional, and in several specimens, taken from the same individual at the

same time, it occurred that in one or two a certain fungus made its appearance and in others it did not. This fact shows that the method employed can not be depended upon for the exclusion of atmospheric germs, but does not affect the value of the result in the considerable number of instances in which no development of organisms occurred in culture-cells in which blood, in a moist state, was kept under daily observation for a week or more.

The method employed seemed the only one practicable for obtaining blood from a large number of individuals without inflicting unwarrantable pain and disturbance upon the sick. It was as follows: One of the patient's fingers was carefully washed with a wet towel (wet sometimes with alcohol and at others with water) and a puncture was made just back of the matrix of the nail with a small triangular-pointed trocar. As quickly as possible a number of thin glass covers were applied to the drop of blood which flowed, and these were then inverted over shallow cells in clean glass slips, being attached usually by a circle of white zinc cement. In dry preparations, which are most suitable for photography, the small drop of blood was spread upon the thin glass cover by means of the end of a glass slip.

The thin glass covers were taken from a bottle of alcohol and cleaned immediately before using, and usually the glass slips were heated shortly before applying the covers, for the purpose of destroying any atmospheric germs which might have lodged upon them. These precautions were not, however, sufficient to prevent the inoculation of certain specimens by germs floating in the atmosphere (Penicillium spores and micrococci); and in nearly every specimen the presence of epithelial cells, and occasionally of a fiber of cotton or linen, gave evidence that under the circumstances such contamination was unavoidable. It is therefore believed that any organism developing in the blood of yellow fever, or of other diseases, collected by the method described, or by any similar method, can have no great significance unless it is found to develop as a rule (not occasionally) in the blood of patients suffering from the disease in question, and is proved by comparative tests not to develop in the blood of healthy individuals, obtained at the same time and by the same method.

Tried by this test it must be admitted that certain fungi and groups of micrococci, shown in photographs taken from specimens of yellow-fever blood collected at the military hospital and preserved in culture-cells, can not reasonably be supposed to be peculiar to or to have any causal relation to this disease.

During my recent visit to Brazil and Mexico I repeated my examinations of blood drawn from the finger of yellow-fever patients, and with the same negative result which had attended similar researches in Havana in 1879. The blood was spread in a thin layer upon clean slides, at the bedside of the patient, allowed to dry at once, and subsequently examined with a DD dry lens and a one-eighteenth inch homogeneous oil-immersion objective of Zeiss. The blood was fixed by heat or osmic acid, and stained with various aniline colors, including methylene-blue, fuchsin, and methyl-violet, all of which colors promptly stain the micrococcus of Freire and similar organisms. I brought back with me numerous slides stained in this way, including some in which the red corpuscles were stained with eosine. The nuclei of the white corpuscles stained by the aniline colors are well brought out, but no micrococci or other bacteria are to be seen in any of these preparations. The following is a record of the cases from which blood was taken for examination in this way:

June 7.—Collected blood from finger in two cases of yellow fever in the Misericordia hospital (Rio de Janeiro). One a Portuguese, an attendant in the hospital, three months in Brazil, in the first day of sickness; the other in the fourth day. Both had highly albuminous urine, and the diagnosis of yellow fever has been made by the house physician. I found them in an isolated ward, from which they were soon after sent to the small-pox hospital, where one of them died.

June 26.—Collected blood from finger of yellow-fever patient in the small-pox hospital; third day of sickness. The patient has highly albuminous urine, and ejected black vomit in my presence. Died the next day.

July 2.—Dr. Araujo Góes, who had assisted me in collecting blood from the above cases, took blood by the same method from the finger of a yellow-fever patient in the small-pox hospital in the sixth day of sickness; a fatal case.

Vera Cruz, September 28, 1887.—Took blood from finger of two patients just admitted to the civil hospital with fever. No parasites of Laveran found on examination of fluid and of stained prepartions. One of these cases seen the following day had al-

buminous urine, a sub-normal temperature, and a feeble pulse of 40 per minute; the surface was cool and moist—second stage of yellow fever. The other also was found without fever; had a slow pulse, a trace of albumen in the urine, and seemed to be convalescent—a mild case of yellow fever.

October 4.—Took blood from case of yellow fever in civil hospital, second day of sickness. *October* 5.—Took blood from same case.

Blood was subsequently examined from two typical cases in the military hospital. The result of all of these examinations, as heretofore stated, was entirely negative, so far as the presence of micro-organisms was concerned.

CULTURE EXPERIMENTS.

The following culture experiments were made with blood drawn from the finger from the four cases above recorded as coming under my observation during my stay in Rio:

In every case the finger was carefully washed, first with a solution of corrosive sublimate of 1 to 1,000, and then with strong alcohol, to remove every trace of the sublimate solution. The puncture was made with a sterilized needle in the palmer surface of the finger near its extremity, and the blood was collected as quickly as possible in little glass tubes with an expanded bulb. A free flow from the puncture was obtained by means of a ligature around the finger, or by pressure applied by the hand. Each capillary glass tube was hermetically sealed in the flame of an alcohol lamp as soon as it was charged with a little drop of blood. The tubes were subsequently taken to the laboratory and the contents used to inoculate the various culture media employed.

July 7.—Blood collected from two typical cases of yellow fever in the Mesericordia Hospital, one in the first day of sickness, the other in the fourth day. From the capillary tubes filled at the bedside I made the following inoculations from each case, viz, two bouillon tubes, two gelatine tubes, one agar-agar tube. *June* 10.—One gelatine tube contains a bacillus, one bouillon tube a micrococcus and actively moving bacilli (vibrios). Another bouillon tube was subsequently found to contain a micrococcus, and at a later date a bacillus also. These micrococci were grouped in tetrads, and did not correspond with the micrococcus of Freire. The remaining tubes remained sterile, viz, two of bouillon, three of gelatine, and two of agar.

June 26.—Collected blood from finger of patient with yellow fever third day of sickness, in the small-pox hospital; a typical case; had highly albuminous urine, and ejected black vomit in my presence. Inoculated at the bedside two bouillon tubes, and at the laboratory six tubes of agar-agar—all of these were placed in an incubating oven (étuve d'Arsonval) in the physiological laboratory at the Museum of Natural History. One bouillon tube "broke down" with the bacteria of putrefaction; the other bouillon tube and the six agar tubes remained sterile.

July 2.—Dr. Araujo Góes, who had assisted me in my previous experiments, collected and brought to the laboratory in capillary tubes blood from a typical case of yellow fever in the small-pox hospital—sixth day of sickness. From these capillary tubes I inoculated three tubes of bouillon and three of agar. In one of the bouillon tubes a large micrococcus in tetrads was developed, and the same large micrococcus*

* The large micrococcus referred to corresponds with the *Tetragenus febris flavæ* of Dr. Carlos Finlay, of Havana, and is very different from the micrococcus presented to me by Dr. Freire as his yellow-fever microbe. I have named it *Micrococcus tetragenus versitilis*, and will give a full account of it in my final report. It is sufficient to say at present that my recent extended researches in Havana show that it is very common *on the surface* of the body of patients in the hospital wards in Havana, and that it is not found in cultures made from the blood and tissues when proper precautions are taken to exclude the possibility of contamination by extraneous organisms.

BALTIMORE, *September* 20, 1889.

associated with a small diplococcus in one of the agar tubes. The other tubes—two bouillon, and two agar—remained sterile.

Vera Cruz, October 12.—Took blood from finger of typical case of yellow fever in military hospital; fourth day of sickness; temperature, 40.5°; urine, albuminous; eyes, yellow. Blood collected in capillary tubes and inoculated at laboratory into five tubes of bouillon, two of gelatine, and three of agar. *October* 13.—Two more agar tubes inoculated with blood from finger of above case. Result: No development of micro-organisms in any of these culture tubes.

It will be seen that the micrococcus of Freire did not develop in any of the tubes inoculated with blood from the finger of five typical cases of yellow fever, and that out of a total of thirty-four culture tubes inoculated twenty-eight remained sterile, while various organisms appeared in six. My inference from these experiments is that the bacilli and micrococci found in these six tubes were present as a result of accidental contamination of the blood drawn, either by organisms on the surface not destroyed by the disinfecting process or by floating atmospheric organisms, attached, perhaps, to epithelial cells or minute particles of wool, etc., which are extremely abundant in hospital wards. This inference is supported by the negative result which attended my direct examination of blood from the same source, and by culture experiments made in Vera Cruz, which show that micro-organisms of the kind encountered are extremely common on the surface of the body of patients in hospital.

The supposition that the micro-organisms present in Dr. Freire's blood-cultures and in those of various other observers who have discovered yellow-fever "germs" came from the surface of the body and not from the blood is sustained by recent experimental researches upon the sterilization of the hands, made by Kümmell* and by Fürbringer.†

These experiments show that it is not an easy matter to destroy all micro-organisms upon the surface of the body by means of a disinfecting solution, and that a simple washing with bichloride solution of one to one thousand does not usually insure sterilization of the hands. Fürbringer, after repeated experiments, recommends the following procedure: (1) Remove all visible dirt from the nails; (2) scrub the hands with soap and water by means of a brush; (3) immerse them for one minute in strong alcohol, at least 80 per cent.; (4) while still wet immerse them for one minute in a 2 per cent. solution of mercuric chloride.

Less thorough treatment did not in Fürbringer's experiments absolutely insure sterilization. In the case of patients in hospital, the difficulty is often increased by the fact that their hands are horny and begrimed with dirt, which can only be removed by long scrubbing.

A character upon which Dr. Freire insists, even in his address delivered in Paris in April, 1887, is the formation of two kinds of pigment, one yellow and one black. From the first he has affirmed that the black color of the characteristic "black vomit" is not due to the presence of blood changed by the acid secretions of the stomach, as has been generally believed by those physicians who have studied the disease, but that this color is due to a pigment produced by his cryptococcus. Now, I have had the coccus which he gave as his yellow-fever germ under cultivation in various media, during a period of several months, and no black pigment has been produced. On the contrary, the colonies in Esmarch tubes, and stick cultures in gelatine, or in agar all have a milk-white color.‡

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* Wie soll der Arzt seine Hände Desinficiren? Deutsche med. Wochenschr., 1886, No. 32, p. 555.

† Untersuchungen und Vorschriften über Disinfection der Hände des Arztes, etc. Wiesbaden, 1888.

‡ BALTIMORE, *September* 20, 1889.

I have repeatedly demonstrated the fact that the colored flocculi which are in suspension in "black vomit" and give to it its characteristic appearance are made

EXPERIMENTS OF DR. DANIEL RUIZ.

If the infectious agent in yellow fever is present in the blood, we would expect that the disease may be transmitted by inoculating a susceptible person with blood drawn from one sick with the disease. Dr. Finlay, of Havana, believes that the disease is commonly transmitted by mosquitoes, which, after filling themselves from a yellow fever patient, transmit the germ by inoculation into susceptible persons. Evidently the most satisfactory and direct way of determining whether the infectious agent is present in the blood would be to make inoculation experiments in susceptible persons. Before going to Brazil I had considered the possibility of making this crucial experiment, and had determined to make it if opportunity offered. When in Vera Cruz I learned that the experiment had already been made in 1885 by Dr. Daniel Ruiz, director of the civil hospital in that city. Dr. Ruiz is an entire unbeliever in the infectious nature of yellow fever, and had no confidence in the alleged discovery of a yellow fever germ by Dr. Carmona, of the City of Mexico. In order to test, in a practical manner, the truth of his views, he made, in 1885, injections of blood and of urine from typical cases of yellow fever, into the subcutaneous connective tissue of an "unacclimated" person. The result of these inoculations was negative. At the time of my visit to Vera Cruz he expressed his entire willingness to repeat these experiments in my presence. This was exactly what I desired, and accordingly Dr. Ruiz made three inoculation experiments upon three unacclimated persons in the hospital. Unfortunately, the blood used for two of these individuals was obtained from a case in which the pathological appearances did not fully sustain the diagnosis of yellow fever made during life. This case is one of great interest with reference to the question of diagnosis, and I shall give a tolerably full account of it. The third inoculation was made from a non-fatal case in the eighth day of sickness; urine still albuminous; skin yellow. Fifty cubic centimeters of blood was drawn from the median vein of this patient by means of a hypodermic syringe, which had been care-

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up of decolorized blood corpuscles; and that the dark color of the fluid is due to a brownish pigment which, without doubt, is altered blood pigment. But inasmuch as this fact is denied by Dr. Freire on the ground that he has failed to obtain the spectrum which characterizes blood pigment, I have thought it best to have a spectroscopic examination made by an expert in researches of this kind. With this view I collected black vomit last summer (1888), in Havana, from a number of typical cases, and placed the material in the hands of Dr. George T. Kemp, Ph. D., of Johns Hopkins University, now of the Hoagland Laboratory, Brooklyn, N. Y. Dr. Kemp has given me the following account of the result of his spectroscopic examination:

BROOKLYN, N. Y., *March* 4, 1889.

MY DEAR DOCTOR: After your departure, I opened the bottles containing the black vomit collected by you last June. The vomit was much decomposed, but in spite of this decomposition the masses of partly decolorized red blood corpuscles could still be made out. A spectroscopical examination proved the existence of blood pigment beyond a shadow of doubt! The reaction of the vomit was strongly *alkaline* from fermentation, and the vomit, untouched by any chemical reagent, gave the spectrum of *alkaline hæmatin*. Boiling this with acetic acid gave the spectrum of *acid hæmatin*, and treating the vomit with Stokes' fluid and ammonia gave the characteristic beautiful bands of Hæmochromogen (Stokes' Reduced Hæmatin). These are the characteristic spectra which one would expect to obtain from decomposed blood, and prove, beyond all question, the presence of blood pigment in the vomit.

These observations agree with those of Dantec, except in one point, viz, that he found the pigment in the condition of hæmaglobin or methæmaglobin. There is not the slightest contradiction here, for he examined the vomit fresh, while the specimens at my disposal had undergone alkaline decomposition, and this process *should* change the hæmaglobin or methæmaglobin found by him into the alkaline hæmatin found by me. Our observations, therefore, are entirely in accord. I only examined the specimens taken from the *stomach;* the specimens of dark colored material from the intestine I shall examine later.

fully sterilized. This was immediately after injected, subcutaneously, in the deltoid region, into the arm of a man aged forty, from the interior of Mexico, who had been in Vera Cruz only twenty days. The man from whom the blood was taken was apyretic, and the experiment is open to the criticism that it was perhaps too long after the inception of the malady. I was, therefore, anxious to make other experiments before leaving Vera Cruz, but the time fixed by my orders expired without my having had an opportunity to do so.

The case in which the autopsy did not sustain the diagnosis was No. 122 in the civil hospital. I quote from my notes as follows:

"Estivan Peris, aged twenty-nine years, three years in Vera Cruz. Taken sick October 1 at 3 o'clock in the afternoon; admitted to hospital October 4, 7 a. m.; conjunctivæ injected; pain on pressure in epigastric region, urine albuminous. Temperature at 5 p. m. 40.6° C. (105.1° F.); no chill at outset; pain in head and limbs.

"October 5, 7 a. m.—Temperature 40.4° C. (104.7° F.); pulse 144. 5 p. m. temperature 38.6° C. (101.7° F.); pulse 136; vomited at 2.30 and at 4.30 a clear acid liquid; urine acid, albuminous. Diagnosis by director of hospital, 'yellow fever.' At this visit (5 p. m., October 5) blood was obtained by cupping from the epigastric region, and of this 40 cubic centimeters was injected into the arm—deltoid region—of a young Spaniard who has been in Vera Cruz about a year and has never had yellow fever. At the same time blood was collected from the finger of the patient and inoculated into four tubes of bouillon and three tubes of agar-agar." There was no development in any of these tubes.

"October 6, 7 a. m.—Temperature 38.7° C. (101.6° F.); pulse 116; urine still albuminous. 6 p. m. temperature 40.7° C. (105.2° F.); pulse 120; pain on pressure over epigastrium and kidneys; conjunctivæ injected; great mental torpidity, hesitation in answering questions; nausea, but no vomiting."

NOTE.—Up to this time the case presented the appearance, and had the history of a case of yellow fever, and I fully concurred in the diagnosis of Dr. Ruiz, director of the hospital.

"October 7, 7 a. m.—Temperature 38.1° C. (100.5° F.); pulse 144; respirations 52 per minute; has strabismus and tonic contractions of the flexor muscles of the arms; conjunctivæ injected and yellow; paralysis of the bladder. A large amount of albuminous urine drawn from bladder by means of the catheter."

NOTE.—The rapid pulse and free secretion of urine are not common in yellow fever at this stage, neither is mental hebetude, in the absence of suppression, or strabismus, and tonic contractions of the muscles met with in my experience. The fall of temperature on the 5th, lasting until the morning of the 6th, and supposed to be that commonly encountered in yellow fever—stage of calm—was followed by an evening exacerbation on the 6th, and a morning remission on the 7th, which gives to the pyrexia a remittent character.

"October 7, 5 p. m.—Strabismus and contraction of flexor muscles more pronounced, hiccough; ineffectual efforts to vomit; does not respond to questions; a large quantity of urine again drawn from bladder—not albuminous—contains granular tube casts and epithelial cells from bladder. Temperature 37.6° C. (99.7° F.); pulse 120. At this visit (5 p. m., October 7) Dr. Ruiz drew from the median vein of the arm of this patient 50 cubic centimeters of blood by means of a hypodermatic syringe, and injected it immediately into the arm of a native of the interior, who had been but twenty days in Vera Cruz."

NOTE.—*The result of the above mentioned inoculations was entirely negative.*

"October 8, 7 a. m.—Temperature 39.3° C. (102.7° F.); pulse 120; a quantity of urine again drawn from bladder; symptoms the same. 6 p. m. Skin cold and moist; unconscious.

"October 9.—Had convulsions during the night: died at 7 a. m. Temperature in axilla one-fourth hour after death 40.3° C. (104.5° F.)

"Necropsy at 7.30 a. m.—Conjunctivæ yellow; skin slightly yellow: temperature

between stomach and liver, ten minutes after opening cavity of the abdomen, above 42.6° C. (108.6° F.), which is the limit recorded by thermometer. There are newly-formed adhesions between the viscera in the cavity of the abdomen, and also between the pleural surfaces. The liver is very large, full of blood, and of a color darker than normal; upon its surface are hemorrhagic infarctions; gall-bladder full of viscid and dark-colored bile. The stomach contains a yellowish liquid, with brown flocculi, which, upon microscopic examination, prove to be made up of desquamated epithelium. Spleen very large, soft, and dark-colored, attached to other viscera by newly-formed adhesions. Pericardium contains 3 to 4 ounces of a yellow fluid." (A culture made from this fluid contains a micrococcus.) I regret that no examination of the intestine was made in this case to ascertain whether there was ulceration of the intestinal glands. At the autopsy I did not hesitate to express my belief that a mistake in diagnosis had been made, and that in my opinion the pathological appearances considered in connection with the clinical history seemed to favor the view that the case was one of bilious remittent fever. Dr. Ruiz, who has made many autopsies, was still of the opinion that the case was one of yellow fever, and stated that in a certain number of cases of this disease which had come under his observation pathological appearances were such as were presented in the case under consideration. A microscopical examination of the tissues, made in Baltimore, has not served to settle the question of diagnosis in a definite manner. The most striking thing encountered in sections of the kidney and liver is an enormous number of leucocytes in the capillary vessels. Dr. William Welch, professor of pathology in Johns Hopkins University, who has kindly looked at my sections, does not hesitate to pronounce the case one of leucocythæmia. Under these circumstances it is evident I am obliged to exclude the inoculation experiments made with blood from this case, and also the culture experiments made with blood drawn during life and from the tissues immediately after death. These, however, have a certain interest, and I accordingly report them here.

At the autopsy I inoculated two agar-agar tubes with blood from the heart, two with material drawn with due precautions from the interior of the liver, two from the kidney, one from fluid in the pericardial sac. Two bouillon tubes with blood from the heart, and two with bile from the gall-bladder. Two days later (October 11) the two tubes from the kidney contained, one a baccillus resembling B. termo, and the other two species of micrococcus. The tube inoculated from the pericardial fluid contained a large micrococcus in tetrads. One of the agar tubes from the liver contained a micrococcus and two bacilli. All of the tubes (two agar, two bouillon) inoculated with blood from the heart remained sterile.

As stated in the introduction to this report, I made preparations before leaving Baltimore to make extended researches, similar to those above reported, by inoculating various culture-media with material taken directly from the interior of the organs chiefly involved in the disease under consideration—especially from the liver and kidney. It was also my intention to make a biological analysis of the contents of the stomach, the intestines, and the bladder. But, unfortunately, the opportunity for carrying out this intention did not occur, and greatly to my disappointment the time allotted to the investigation with which I was charged expired without my having been able to carry out my plans in this particular.

EXAMINATION OF TISSUES.

In all infectious diseases which have been proved to be due to the presence of a parasitic micro-organism in the blood, this organism may be demonstrated in properly stained thin sections of the tissues. In such sections we often obtain cross-sections of small blood-vessels in which the blood corpuscles are *in situ*, and in which a stained micro-organism, if present, would be very apparent. We also have a satis-

factory view of the contents of the capillary vessels of the liver, kidney, brain, etc., in well-prepared sections of these organs. Pathologists, therefore, look upon a careful research, by the methods which have been perfected with this object in view, as of prime importance in any attempt to prove whether a given infectious disease depends upon the presence in the blood of a specific micro-organism. Moreover, in certain infectious diseases in which a parasitic micro-organism has been proved to be the essential etiological factor, this organism is not found, as a rule, in the general blood current, but is present in the tissues especially implicated in the morbid process, *e. g.*, in typhoid fever in the spleen and intestinal glands, in tuberculosis in the tubercular nodules in the lungs and elsewhere. Failure to find a parasitic organism in blood drawn from the finger is therefore not satisfactory evidence of the absence of a specific germ from the tissues of the organs involved.

As in yellow fever the liver and the kidneys give evidence of pathological changes resulting from the disease, I have naturally given special attention to these organs in the researches I have made.

Before recording the results of my own recent researches in this direction I desire to quote from the preliminary report of the Havana yellow-fever commission, submitted November 18, 1879.

Morbid anatomy and pathological histology.

In the division of labor made by the commission at the outset of the investigation this portion of the work was assigned to Dr. Guitéras, who reports as follows:

Twenty-two autopsies have been performed during the months of July, August, and September, 1879. Of these eighteen have furnished material for histological studies. All the post mortems but two were performed at the military hospital of San Ambrosia. The diagnosis of the disease was confirmed in every case by the attending physician, and frequently also by the director of the hospital. In this institution the material for the study of the morbid anatomy of yellow fever is amply sufficient. The commission has met with no obstacles in the discharge of its duties, both because of the favorable disposition of the physicians in charge and because of the absence of all fears of contamination on the part of the community.

Rather than conclusions, the statements presented in this report should be considered as suggestions brought forward by a preliminary examination which your committee expect to substantiate after further investigation.

The organs that have been prepared for examination are: The liver, stomach, and intestines, the kidney, the supra-renal body and the spleen, the spinal chord, the medulla oblongata, the meso-encephalon, the pneumogastric nerve, and the semilunar ganglion of the abdomen, the heart and other muscles, the mesenteric glands, and the lungs.

The tissues from fourteen of the cases are already cut and ready for mounting. Of the first eight cases a number of sections have been mounted (144) and accompany this report.

1. *The liver* has been found always to be of about the normal size and consistency. Its color in the majority of the cases light, the exceptions being one case of chronic cirrhosis and two cases in which the lungs were found studded with hemorrhagic foci. The lesion constantly found in the organ by microscopic examination is the so-called parenchymatous inflammation of Virchow. The hepatic cells are found in a condition of cloudy swelling. Besides the fine albuminous granulation, the cells show at times evidences of fatty degeneration and pigmentary infiltration. As in other cases of parenchymatous inflammation, here also the connective tissue is found to partake of the general nutritive change. It is swollen and presents some embryonal cells. This is very apparent in one case where the lesion occurs in a liver previously affected with chronic cirrhosis. In this case the adult connective tissue is abundantly infiltrated with young inflammatory tissue.

The larger biliary passages are found patulous throughout, and the smaller ducts present no evidences of catarrhal inflammation: so that if any obstruction exists in the latter it is due to the cloudy swelling of the hepatic cells and the interlobular connective tissue. It has been supposed that the jaundice may be due to diminished pressure in the portal circulation; yet, in spite of the depletion by hemorrhage from the portal radicles, the interlobular veins are found sometimes choked up with blood.

No microphytes have been found in the liver or in the blood contained in its vessels.

2. *The stomach* presents no evidence of inflammation. The protoplasm of the epithelial cells is normal, and the nuclei quite distinct. There is no degeneration of the

muscular coat. It is very difficult at first to find the source of the blood found in the black vomit. The reason is this: That the tops of the ridges between the gastric follicles are removed by post-mortem digestion, and it appears that the hemorrhages take place always, as far as I have seen, from the loops of capillaries that rise into these ridges. The post-mortem digestion removes therefore the hemorrhagic foci that could lead us to detect the points of hemorrhage. In some of the preparations, especially those stained with hæmatoxylon, where these tops remain, small hemorrhagic infarctions may be detected close under the free surface of the mucous membrane. In confirmation of this supposed action of post-mortem digestion may be mentioned the fact, which was to be expected, observed by Dr. Sternberg, that the black vomit examined ante mortem presents scarcely any cylindrical epithelium, while the fluid contained in the stomach after death is crowded with it.

3. *The kidney.*—No autopsy has been made before the third day of the disease. In all cases the epithelial cells are more or less in a state of cloudy swelling. Sometimes they seem to be large enough to obstruct the lumen of the tubules. In every kidney, however, some tubules are met with which appear to be in a normal condition. In some of them, on the contrary, there are evidences of catarrhal inflammation; some young cells are met with displacing the older ones, and some round cells are found between the tubules. Not infrequently yellow casts are encountered, choking up the caliber of the tube. The blood vessels, especially toward the cortex, are quite frequently distended with blood. Some of the tubules also contain masses of coagulated blood. *No organisms have been found in the kidney.*

4. *The heart.*—The examination of this organ shows that there is no foundation for the opinion that there is a fatty degeneration of the muscular fiber. The heart is almost always found firmly contracted, and its consistency and color are normal. The striations are always distinct and only in some of the fibers a few fatty granules are found in the neighborhood of the nuclei. The *rectus muscle* and the *diaphragm* are found in normal condition.

5. *The semi-lunar ganglion.*—Connective tissue of new formation is here met with to a greater extent than in the tissues heretofore described, but the nervous elements present no evidences of degeneration further than the cloudy swelling already described in other organs.

Of the other portions of the nervous system, which have not been examined microscopically, it may be said that they present nothing abnormal to the naked eye.

As the methods of staining employed by Dr. Guitéras in Havana were not as satisfactory for the demonstration of micro-organisms as some which have since been devised, I have not considered our failure to find micro-organisms in sections of tissues mounted by him at that time as sufficient evidence of their absence. We could, however, scarcely have failed to see, by the methods used, a micrococcus like that which Freire presented to me in Rio as his yellow-fever germ, or anything like the micrococcus in tetrads which Dr. Finlay, of Havana, believes to be the specific cause of the disease.

Desiring to supplement the observations made in Havana, in 1879, by further researches, I wrote to my friend Dr. Daniel M. Burgess, of Havana, some time during the summer of 1884, requesting him to obtain for me small pieces of liver, kidney, and stomach, from one or more typical cases of yellow fever. I made it an essential condition that the autopsies should be made within an hour, or, at the outside, two hours after death, so that there might be no question of *post-mortem* changes. Small pieces of the organs named were to be put at once into a large quantity of strong alcohol. In compliance with my request, Dr. Burgess obtained and forwarded to me material from two cases which reached me in good condition, and, upon microscopic examination, the liver and kidneys showed the pathological changes constantly found in the disease in question. During the winter of 1884 I mounted numerous thin sections from this material, stained with various analine colors. In none of them did I find any micro organisms, except upon the surface of the mucous membrane in sections of the stomach, where various organisms—bacilli and micrococci—were to be seen in properly stained sections. These were, however, only upon the surface, attached to the epithelium, or mingled with a granular debris adhering to the surface of the mucous membrane. In the autumn of 1885, during a visit to Dr. Koch's laboratory in Berlin, I had an opportunity to avail myself of the suggestions and valuable assistance of the Master in Bacteriology, and again studied the material which Dr. Burgess had

sent me from Havana, by the various methods of staining considered to be most useful in such a research. At the request of Dr. Koch I was assisted in this research by Dr. Carl Seitz, who was at the time engaged upon his studies of the typhoid bacillus, and was an expert in staining and mounting thin sections of the tissues. Dr. Seitz and myself examined numerous sections of liver and kidney stained by various methods, with an entirely negative result so far as the presence of micro-organisms was concerned. After my return to Baltimore, in 1886, I again made numerous sections from the same material, and stained them with Loeffler's alkaline solution of methyline blue, which we had also used in Dr. Koch's laboratory, and with other aniline colors, but without any better success.

Desiring to repeat these researches upon fresh material, I wrote to my friend Dr. Burgess, during my stay in Rio (June and July, 1887), requesting him again to collect pathological material for me from at least four cases of yellow fever, so that after my return to Baltimore I might continue these investigations. As before, this material was to be obtained as soon as possible after death, and to be put at once in strong alcohol. About the 1st of December I received from Dr. Burgess the desired material in good condition, together with the following letter:

HAVANA, *November* 19, 1887.

MY DEAR DOCTOR: I send you, per Dr. Spore, of *City of Washington*, which sails today, one box of pathological specimens. * * * You can rely implicitly upon the specimens having been taken from well-diagnosticated yellow-fever cases, at the time *post-mortem* stated on the bottles. All had, besides the proper temperature curve, irritable stomach, black vomit, highly albuminous urine, eventually in most cases suppression of urine, etc. I saw them repeatedly.

The bottles were marked as follows:

Case No 1.—Sick from August 14 to 19, 1887. Autopsy one hour after death.

Case No. 2.—Died September 23, 1887, at 4.30 a. m. Autopsy two and one-half hours after death.

Case No. 3.—Died October 5, 1887, 2.30 a. m. Autopsy fifteen minutes after death.

Case No. 4.—Died October 26, 1887, 5.30 a. m. Autopsy 7 o'clock a. m., body still warm (temperature 40° C.)

From the above-described material I have had made a large number of very thin sections, which I have studied by various methods of staining and with objectives of high power—the one-eighteenth and one-twelfth inch hom. ol. im. of Zeiss. I have used especially the alkaline solution of methyline blue of Loeffler; Gram's well-known method, with methyl violet, followed by iodine solution and decolorization with alcohol; the method of Weigert, which is the same as Gram's up to the point of removing the sections from the iodine solution, when they are decolorized and dehydrated with a mixture of two parts of aniline oil to one part of xylol. I have been especially pleased with the last-mentioned method, which gives fine views of the tissue elements and any micro-organisms which may be present. I also stained numerous sections with fuchsin, in solution with carbolic acid (5 per cent.), with analine oil (tubercle stain), and with various other aniline colors.

I think I am safe in asserting that all known pathogenic micro-organisms may be stained by one or more of the methods above referred to. Indeed, the alkaline solution of methyline blue is, so far as I know, an agent which stains all organisms of this class, although there are differences as to the rapidity with which they stain and the tenacity with which they retain the color imparted to them.

The result of this research has again been negative so far as the *general* presence of any particular micro-organism in the material examined is concerned. But in one case (No. IV) I found in the kidney a minute bacillus, which apparently invaded by preference the glomeruli. It was not found in the capillaries generally, but a certain number of foci were found, some small, as shown in Fig. 2, and involving only a portion of a glomerulus, others involving a whole glomerulus and the tissues immediately surrounding it. The appearance was such as one would expect to see in a case in which solitary bacilli, carried in the first place by the blood-current, had

effected a lodgment and established a center of infection in tissues already, perhaps, necrotic, and through which the circulation had ceased. The latter supposition seems to be justified by the fact that there were comparatively few of these foci, whereas if they had been established while the circulation was still going on we would expect to find numerous secondary foci and a certain number of bacilli in the neighboring capillary vessels. Moreover, there was no evidence of inflammatory reaction as a result of this invasion of the tissues by parasitic organisms. I am, therefore, of the opinion that this is some ordinary saprophyte which had effected a lodgment in the kidney, possibly during the last hours of life when the vital resistance of the tissues was slight, or when, as a result of the blood stasis in the organ, local necrosis had already occurred at certain points before death. It is quite probable that during the last hours of life a certain number of micro-organisms from the intestine succeed in passing through the enfeebled tissues to the interior of the capillaries, and are carried away by the already slowly moving blood-stream to distant organs, where they may establish centers of growth even before death occurs, or are at least in position to take possession of the field as soon as the vital spark has been extinguished. In the case in question I believe that the true explanation of the presence of the organisms described is that suggested, for I have not found in the other cases examined any similar collections of bacilli, and can not therefore attach any impor-

FIG. 2.—Collection of Straight Bacilli in Glomerulus, yellow fever kidney. Material from Havana. × 450.

tance to the observation so far as the etiology of yellow fever is concerned. In Berlin I fell upon a little group of minute, slender bacilli, in a capillary of the liver, and recently I have found a similar group in a preparation of skin from a yellow-fever patient. I have also in the course of my extended observations seen two or three groups of micrococci or of what appeared to be micrococci. But I attach no importance to such observations. Evidently any organism concerned in the etiology of an infectious disease should be found not occasionally and in certain cases only, but, if

seen at all by the staining methods adopted, it should be found distributed through the organs involved in sufficient numbers to leave no doubt as to the presence, not as an accident, but as a general and constant thing in all cases of the disease under investigation.

The bacillus above described, present in a single case, is, then, the only micro-organism found in the material obtained in Havana, so far as the liver and kidney is concerned. In my stained sections of stomach and intestine I have observed various micro-organisms, upon the surface of the mucous membrane, but extended researches have failed to show that any one of these organisms invades the living tissues of the alimentary canal.

While in Brazil my friend Dr. Goes gave me material from nine cases in which he had made the autopsies during the epidemic of 1884, and which had been in the physiological laboratory of the Museum of Natural History (Dr. Lacerda's laboratory) since the date mentioned. Since my return to Baltimore I have mounted thin sections, stained by Gram's method and Loeffler's alkaline solution of methyline blue, from each of these cases. In two I find in the capillaries of the liver and of the kidneys an organism which has been described by Babes and by Lacerda, who found it in material collected at the same time and probably from the very same cases as those in which I now find it. This micro-organism is a short bacillus, which occurs in chains, as seen in Fig. 3.

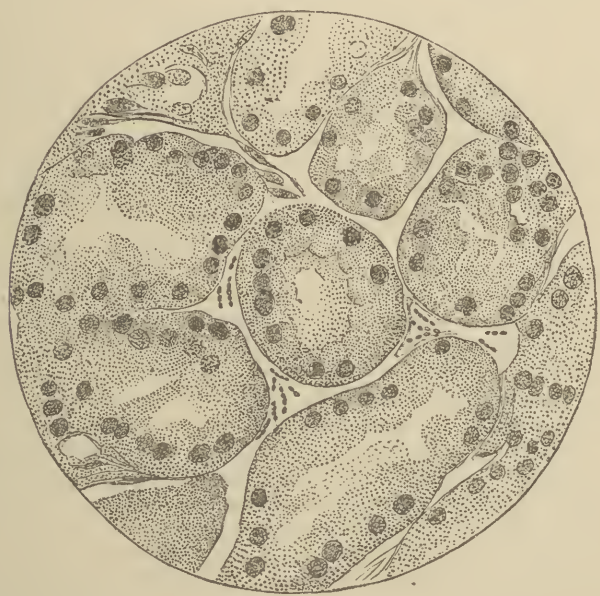

FIG. 3.—Bacillus of Babes in kidney, yellow fever. Material from Dr. Lacerda's laboratory in Rio Janeiro. × 450.

In certain places, especially in the kidneys, it is found in the capillaries in great numbers massed together; in other places it is distributed more sparsely, as seen in the figure. Careful examination of specimens stained with Loeffler's solution shows that the separate elements in these little chains vary considerably as to their length and that the ends are more deeply stained than the center. This appearance was no doubt observed by Babes, who first described the organism in question, but he has interpreted it differently. He says:

"These filaments appear united and homogeneous with an amplification of 600 diameters, but with a high power (one-twelfth hom. im., or No. 12 of Verick, which corresponds with the one-eighteenth of Zeiss) one can assure himself that these filaments are composed of elliptical grains, almost cylindrical, arranged in pairs, forming little groups in which they are united by an intermediary pale substance. The filaments are thus composed of diplococci, or, if one wishes, of very short rods with terminal spores." (*Op. cit.*, p. 522.)

Dr. Lacerda has described the organism referred to as in filaments which branch dichotomously, and believes this branching to be a constant and distinctive character of the parasite which he accepts as the veritable yellow-fever microbe. He is without doubt mistaken. The apparent branching of the filaments which he has described and drawn, and which he showed me in some of his preparations at the time of my visit to Rio, is due simply to the accidental juxtaposition of the torula-like chains. He is also mistaken in supposing that this organism is only to be satisfactorily demonstrated by Gram's method of staining. My friend Dr. Goes shared this belief at the time of my visit to Rio, but I demonstrated to him the facility with which the organism may be stained with a solution of methyline blue, upon sections which he made for me from material in Dr. Lacerda's laboratory. Since my return to Baltimore I have made numerous sections from the same material (two cases out of the nine) and find no difficulty in staining the organism present in the tissues with methyline blue or with fuchsin. Dr. Goes also supposed that his failure to find this parasite in all of the tissues which he had preserved since the epidemic of 1884 was due to the fact that the tissues had been kept too long. He thought that it was most easily stained in recent tissues, and anticipated that when he had again an opportunity to make autopsies he would encounter this micro-organism in the tissues. I shall await with interest his report of his recent researches. As already stated, I have not been able to find this microbe of Babes in the tissues of six undoubted cases of yellow fever sent to me from Havana, and examined most carefully within six months of the date of the autopsies. Babes himself has renounced the idea that this micro-organism bears an etiological relation to the disease under consideration. In the second edition of "Les Bactéries" he says: "Since these researches we have had the opportunity to examine several series of sections from yellow fever; first, the liver and kidneys of two individuals dead from this malady, collected by Dr. Alvarez, were examined in the laboratory of pathological anatomy of the faculty of Paris without any bacteria having been found; second, material from three cases of yellow fever which Koch was kind enough to confide to one of us. In these three last cases, notwithstanding the most scrupulous research, and notwithstanding the advice of Koch, it was impossible to find the little chains in the brain, the kidneys, the liver, and the spleen. We must suppose, then, that in yellow fever, as in other infectious maladies, microbes are only found in the parenchymatous organs in certain cases and not in all. The question whether these micro-organisms really constitute the cause of the malady, or simply a complication, is consequently not resolved."

We would remark that in view of the negative results attending Babes's more recent researches, and our own extended study of the tissues from six typical cases occurring in Havana, there is no good reason for supposing that the above described micro-organism bears an etiological relation to yellow fever. On the contrary it seems probable that its presence in material from a limited number of cases occurring in Rio is either entirely accidental or is due to a secondary complication, perhaps to some form of septicæmia. Babes has recorded the following observations with reference to his examination of the intestine:

"According to the examinations made in the three last cases of yellow fever there were in the various liquids secreted, and especially in the intestine, several species of micro-organisms. Thus in two cases we found in extended portions of the mucous membrane of the small intestine in the glands and below them short bacilli, which

resemble those of typhoid fever, but in which the large spores were often terminal. They have portions of their protoplasm but slightly colored and their extremities were a little attenuated. In one of these cases the mucous membrane was very much altered in places, had lost its epithelium and was hemorrhagic. Its superficial part was necrosed and yellow as far as the level of the glandular cul-de-sac, and the structure of the tissue could no longer be distinguished. Below the glandular layer we noted an infiltration of round cells and some of the culs de-sac of the dilated tubular glands inclosed often dense masses of the bacilli above described.

"In another case there were shorter bacilli, sometimes in pairs, in small number, either upon the surface of the intestine or in the glands. In the contents of the intestine we found in two cases dense masses of large spherical microbes of about 1 μ, inequal, near which there existed always brown or yellow pigment. The urine contained in one of these cases the same agglomerations of large spherical microbes without yellow pigment, and in the two other cases a quantity of pear-shaped monads, 2 μ in thickness and 3 to 4 μ long, possessing a slender extremity. These monads, free, isolated from each other, easy to color with the aniline colors, contained large vacuoles. Some were in process of division. The wall of the bladder was very thick and the mucous membrane had lost in places its epithelium and was infiltrated with leucocytes. The monads penetrated between the epithelial cells. Thus it is probable that the great quantity of monads observed was in relation with the inflammatory lesions of the bladder. Alvarez has shown us drawings of micro-organisms which he has observed in the urine and which represent little chains comparable to those which we saw in our first examination of the kidney.

"Our knowledge of the micro-organisms of yellow fever is reduced, as may be seen, to a very small matter; from the histological examinations which precede we can not be sure that the micro-organism observed in our first researches is that of yellow fever. It has neither been isolated nor cultivated, and the experiments which up to the present time have been made in Brazil do not merit great confidence." (*Op. cit.*, p. 530.)

Babes is no doubt right in not attaching any special importance to the presence of the micro-organisms observed by him in the intestine and in the bladder. The bacilli with a single spore, according to his account, were found in necrotic tissues, and I have failed to find the same organism in the mucous membrane of the intestine of the four cases recently examined by me. The observation with reference to monads in the bladder is interesting, but it is probable that the inflammation of this viscus was of a chronic character and antedated the attack of yellow fever. Babes says that the mucous membrane was thickened and infiltrated with leucocytes. I have carefully examined sections of stomach from six cases, and of intestine from four. In all the material was put into strong alcohol within a brief period—fifteen minutes to two and a half hours—after death. The epithelium is generally detached, as is usual in the stomach obtained from autopsies in which it is in no way involved, when an interval of some hours has elapsed after death, but in one of my cases, in which the autopsy was made within fifteen minutes after death, the cylindrical epithelium is seen in the sections beautifully preserved, and *in situ*. In *case* 1, from Havana (1887), I find in the mucus and desquamated epithelium attached to the surface of the mucous membrane:

(*a*) A large bacillus with square ends, very abundant.

(*b*) Agglommerations of large oval cells, solitary, in pairs, and in short chains, 4 to 6 μ in diameter—a torula.

In *case* 2 (Havana, 1887), I find upon the surface of the mucous membrane of *stomach:*

(*a*) A few short oval bacilli in pairs or short chains, resembling in form and dimensions those of Babes.

(*b*) A few larger oval bacilli in pairs.

(*c*) A very few micrococci.

In the same case in mucus and desquamated epithelium in the *intestine:*

(*a*) Very numerous short oval bacilli in chains, resembling those of Babes.

(*b*) Numerous large bacilli with slightly rounded ends.

Case 3 (Havana, 1887.) Surface of *stomach:*

(*a*) Numerous small oval bacilli in pairs and chains, resembling those above described.

(*b*) Slender straight bacilli in pairs, not numerous.

(*c*) A few micrococci.

Surface of *intestine:* The same oval bacillus in chains, and large straight bacilli with square ends.

Case 4 (Havana, 1887.) Surface of *stomach:* Cylindrical epithelium *in situ.* Very few micro-organisms observed. *Intestine:* Numerous stained masses of irregular form, and differing greatly in size, 4—12 μ.

Case 5 (Havana, 1887.) Surface of *stomach:*

(*a*) Small oval bacilli in pairs and chains, numerous.

(*b*) Masses of micrococci.

(*c*) A few large bacilli.

Surface of *intestine:*

(*a*) Masses of very minute micrococci and slender bacilli.

(*b*) Large spherical organisms in chains.

I am unable, from the above observations, to fix upon any micro-organism as constantly present, but consider the presence of oval bacilli in chains, resembling those found by Babes in the liver and kidney of certain cases occurring in Rio de Janeiro, as worthy of note, especially as I find this organism in abundance in the stomach or intestine in three out of five cases examined. I am not, however, willing to attach undue importance to this observation, and indeed am not positive that the organism is in all cases identical. Evidently the only way to arrive at facts from which definite conclusions can be drawn will be to make an extended series of culture experiments with material from the various organs, from the stomach, and from the intestine; to isolate the various micro-organisms encountered and to test the pathogenic power of those which there is reason to think may possibly be concerned in the etiology of the disease under investigation.

EXPERIMENTS UPON ANIMALS.

The exactions of modern science require the experimental demonstration of specific pathogenic power by inoculation into a susceptible animal, before a micro-organism associated with a specific morbid process can be accepted as the essential agent in causing the disease. In the infectious diseases of the lower animals, or those which are common to man and certain of the lower animals, *e. g.*, anthrax, glanders, tuberculosis, such proof is easily obtained. But there are certain infectious diseases of the lower animals, *e. g.*, pleuro-pneumonia of cattle, to which man has no susceptibility, and on the other hand there are certain infectious diseases of man, which, so far as we know, can not be transmitted to any one of the lower animals. Evidently in an experimental research it is desirable to ascertain at the outset whether any of the lower animals are susceptible to the disease under investigation, so that, if possible, the *experimentum crucis*, by inoculation, may be made. An attempt was made by the Havana Yellow-Fever Commission (1879) to ascertain whether any of the common domestic animals, available for experimental purposes, are susceptible to yellow fever. In the preliminary report of this commission the writer has given the following account of the experiments made:

It has been commonly reported, and is asserted by several writers of acknowledged ability, that during the prevalence of yellow fever certain of the inferior animals exhibit symptoms of sickness which are attributable to the influence of the yellow-fever poison.

(*Vide* Barton, cause and prevention of yellow fever, third edition, pp. 52–55; Fe-

raud, de la fiévre jaune à la Martinique, p 271; La Roche on yellow-fever, vol. 2, pp. 316–318; Blair, yellow-fever epidemic of British Guiana, third edition, p. 63.)

In view of these reports, the commission was instructed as follows:

"It is obvious that if it be found possible to produce some specific symptoms in some one of the lower animals by exposing such animals in localities known to be capable of producing the disease in man, and thus to establish a physiological test of the presence of the cause of the disease, we may even hope to be able to determine the nature of and the natural history of this cause, although prolonged investigation may be necessary to effect it."

The commission has endeavored to carry out the views of the National Board of Health in this direction, but in consequence of the limited time at its disposal, the want of a suitable place to keep the larger animals, and the amount of work in other directions expected from it, it has been found impossible to make an exhaustive experimental investigation. Enough has been done, however, to make it appear highly probable that the sickness and mortality reported among animals during the prevalence of yellow-fever epidemics has been improperly ascribed to the influence of the yellow-fever poison. It is well known that many of the inferior animals suffer from epidemic diseases peculiar to their several species, and this is especially the case in southern latitudes. We know of no reason why such epidemics should not occur coincidently with yellow fever in man, and it is not surprising that many people unaccustomed to close observation should attribute the sickness in man and in the animals affected to the same cause. In advance of any experiments designed to test the truth of such a deduction, it seemed quite improbable, from the fact that the supposed effect only results exceptionally, if at all, while domestic animals are frequently exposed in large numbers, in localities visited by severe epidemics of yellow fever, without exhibiting any symptoms of sickness. This fact is vouched for by many competent observers and is verified by the personal experience of two members of this commission.

Nevertheless, in view of the reports referred to, of the great importance in the prosecution of the investigation of a test of the presence of the poison, and of the possibility that by close observation and the use of the clinical thermometer some symptoms heretofore overlooked might be discovered sufficient to serve as such a test, it was evidently imperative that experiments should be tried in this direction. Arrangements were accordingly made before leaving New York for a supply of animals as required, and on the 24th of July the following were received per steamer *Niagara*, viz: Four dogs, two cats, six rabbits, six guinea-pigs, one monkey, six chickens, twelve pigeons, and two geese. Subsequently (August 30) six more dogs were received.

All of these animals were carefully observed, and various experiments were tried for the purpose of testing their susceptibility to the influence of the yellow-fever poison. The details of these experiments are given in a special report to the National Board of Health, dated October 15. It is not deemed necessary to give these details in the present report, but the general statement may be made that the results were negative. No symptoms were produced in any of the animals experimented upon which can fairly be attributed to the influence of the yellow-fever poison.

The clinical thermometer was constantly used for the purpose of recognizing any slight febrile movement which might possibly occur, and the blood was examined microscopically from time to time. As the experiments made gave no promise of positive results, the commission did not feel justified in giving more time to this portion of the investigation. It is, however, of the opinion that the reports heretofore referred to and the importance of a physiological test of the presence of the poison would justify the National Board of Health in pursuing this inquiry in future, especially with such animals as this commission has not experimented upon. A few experiments are here given as examples of those made:

"*Experiment No.* 1.—On the morning of July 28, four days after arrival in Havana, the following animals were exposed on board the infected brig, *John Welch, jr.*, viz: two dogs, two cats, one monkey, two rabbits, three Guinea pigs, two geese, three chickens. The time of exposure was forty-eight hours, at the expiration of which time the animals (in cages) were brought back to the laboratory. The *Welch* was a very foul ship, and was loaded with molasses. During the time the animals remained on board six of her crew (all) were down with yellow fever. After bringing the animals back to the laboratory the temperature of each was carefully taken, and daily observations were continued for some time after. No symptoms of sickness presented themselves except in the case of one dog. This animal suffered a sharp attack of fever, but it is believed that the case was one of a disease common to imported dogs in Cuba known as *romadizo*, a disease the clinical history of which is very different from that of yellow fever. (See special report to National Board of Health, dated October 15, for full history of this case.)

"*Experiment No.* 4.—Injected yellow-fever blood, 1½ drams, of first day into femoral vein of dog No. 3. Blood obtained by cupping from patient in civil hospital

and mixed with a small quantity of soda bicarb., to prevent coagulation; *result* entirely negative.

"*Experiment No.* 10.—One-half of a blanket from a yellow-fever patient's bed was placed in the cage with dog No. 4 and left there for several days. *No result.*

"*Experiment No.* 11.—Dog No. 5 was allowed no water for two days, except a supply in which the other half of this blanket (Experiment No. 10) had been washed. *No result.*"

More inoculation experiments would have been made in Havana, if any microorganism had been found in the blood, but in the absence of any evidence that the animals brought from New York were susceptible to the yellow-fever poison when exposed to the conditions under which man contracts the disease (Experiment No. 1), and on account of the limited time at my disposal, I did not follow up this line of investigation.

EXPERIMENTS OF DR. FREIRE.

We quote as follows from Dr. Freire's principal work ("Doctrine Microbienne de la Fièvre, Jaune, 1885"):

"My first experiments made upon the monkey and the dog gave a negative result" (p. 35).

"I have also inoculated black vomit into a dog, repeating the injection twice, at intervals of some days. * * * No phenomenon indicative of yellow fever manifested itself" (p. 36).

"Fowls and pigeons also enjoy a complete immunity, as we shall see further on. After having inoculated these animals with blood drawn directly from the corpses of yellow-fever patients, and also with cultures of different degrees of transplantation, without having succeeded in any case in transmitting to them the malady, I turned my attention to other animals, to rabbits and to guinea-pigs."

"My attention was especially called to guinea-pigs because a merchant of the place said to me that just when the epidemic had attained its maximum of intensity he supported an enormous loss on account of the *peste*, which killed each day a great number of his guinea-pigs" (p. 36).

We remark that the guinea-pig is very subject to various forms of septicæmia, and that those who have endeavored to raise them in latitudes where yellow fever does not prevail have often experienced heavy losses, especially during hot weather and when their cages are not carefully cleaned. My guinea-pigs in Havana did not contract yellow fever, although they were exposed on an infected ship during the hottest part of the year for a period of forty-eight hours. Moreover, Dr. Freire himself gives evidence that during the winter months he inoculated these little animals with blood from yellow-fever patients without result. He says:

"The influence of season upon the evolution of the microbe of yellow fever is very powerful. For the purpose of determining the nature of this influence we have proceeded to various experimental researches. We have inoculated a large number of guinea-pigs, not only by the method of vaccination but also by sub-cutaneous injection of cultures of the microbe in gelatine. These cultures showed themselves fertile in characteristic organisms, and their energy had already been proved, since their inoculation had caused the death of several animals. Very well, these inoculations made in July and August have given only negative results. The animals presented a slight elevation of temperature, but survived the consequences of the inoculation. Even the blood of patients sick with yellow fever transported [inoculated] into animals in the months of July and August could not cause their death. Indeed, on the 15th of August we have injected with the blood of a patient attacked with yellow fever nine guinea-pigs. The following is the course of the temperature as observed:

No.	Before the experiment.	After injection.			
		July 16.	July 17.	July 18.	July 19.
	°	°	°	°	°
1.....	38.9	39.0	37.8	38.2	39.0
2.....	38.8	38.7	39.0	39.0	39.6
3.....	39.0	39.0	38.0	38.4	38.8
4.....	38.6	39.9	38.9	38.8	38.6
5.....	39.0	39.2	38.0	39.0	39.0
6.....	38.8	39.0	38.8	39.8	40.0
7.....	39.1	39.0	38.5	38.9	39.4
8.....	39.2	39.2	37.4	39.0	38.5
9.....	38.8	38.2	39.6	39.2	38.5

"The following days the temperatures of nearly all of these animals became normal. None of them died. This fact shows the innocuity, due to a change of season, of the inoculations which a month previously showed themselves virulent and so toxic that they infalibly caused the death of all the animals" (p. 235).*

Dr. Freire has referred to the experiments of Dr. Rangé, "Médecin de premiere classe," of the French navy, as confirming his own. These experiments were made during an epidemic which occurred in 1885, upon the Iles du Salut (Guyane).

The inoculation experiments of Dr. Rangé were made *during the height of the epidemie*, in the month of April. He says:

"In guinea-pigs inoculation of blood taken directly from the patient was not followed by any result. Inoculations with *black vomit, cultures from blood, or cultures from black vomit* gave always a positive result—that is to say, they were followed by reactional phenomena; four times they determined death."

These cultures, like those of Dr. Freire and others obtained from the same source, no doubt contained various organisms, and among them one or more may have been pathogenic for the guinea-pig, but the experiments made show most definitely that blood drawn directly from the patient *during the epidemic season* does not kill guinea-pigs. We must therefore conclude that the death of guinea-pigs inoculated by Dr. Freire during the epidemic season resulted not from yellow fever, but from inoculation with some pathogenic organism, which was abundant during the summer months, and consequently was present in his cultures, or from accidental inoculation through the wound made by him in his experiments. The guinea-pig is very subject to the last-mentioned accident, especially when kept in foul cages. Its own discharges, and the remnants of food in its cage furnish a patulum in which a multitude of micro-organisms are to be found. Owing to the shortness of its legs its abdomen is constantly soiled with this material, and if any pathogenic organism is present, an inoculation wound made for experimental purposes can scarcely fail to be infected with it.

It is scarcely worth while to give in detail the experiments upon guinea-pigs made by Freire, in which death followed the inoculation, and in every one of which the assumption is made that the animals succumbed to yellow fever. But his summary statement of these experiments presents some points of interest. Thus we find that one animal died at the end of a few hours, while one lived for thirty days. Yet death in both of these extreme cases is ascribed to yellow fever, resulting from the inoculation practiced.

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* In Havana, during the past *summer*, I have inoculated a number of guinea-pigs with blood from the heart and with material—blood and crushed tissue elements—from the liver of yellow-fever cadavers, and have always had a negative result when the autopsy has been made very soon after death. On the other hand, I have found that material from the liver which had been kept in the laboratory for some time is very virulent. A full account of these experiments will be given in my final report.

BALTIMORE, *September* 20, 1889.

The following résumé is given:

	Animals.
Duration one to three days	9
Duration four to eight days	8
Duration nine to fifteen days	5
Duration more than fifteen days	1

Dr. Freire remarks that in the case of four animals the duration of the malady can not be precisely determined, inasmuch as they died spontaneously, *i. e.*, without having received an inoculation. In these cases also Dr. Freire infers that the cause of death was yellow fever, and in all of the autopsies he finds evidence satisfactory to himself that such was the fact. I shall not attempt to analyze this evidence in detail, but quote that relating to the color of the liver alone. Pathologists are generally agreed in considering the color of the liver in yellow fever, due to fatty degeneration of the organ, as the most characteristic pathological appearance. In man the liver has a color which has very aptly been compared to that of new leather. Now, in Freire's summary statement of the color of this organ in his inoculated guinea-pigs we find (p. 178) that it was blackish (*noirâtre*) seventeen times; bronze color in one case; punctate with yellowish white, once; straw color, once; with pink spots, once; color not mentioned, six times.

I shall quote here a single experiment in which a fatal result occurred, and in which, as usual, Dr. Freire ascribes death to yellow fever resulting from the injection, notwithstanding the fact that the material injected (blood) had been subjected to a boiling temperature for some minutes. My own numerous experiments show that all known micrococci are quickly destroyed by a temperature much below the boiling point of water.*

Dr. Freire's account of this remarkable experiment is as follows:

"We must note that the microbe of yellow fever offers a remarkable resistance to heat. The following experiment furnishes a demonstration of this:

"On the 17th of April, 1883, we subjected to ebullition for several minutes a gram of blood containing the microbes. We injected it afterwards into a guinea-pig, which had a temperature before the experiment of 38.5° in the axillary region. The temperature followed this mark the following days: April 18 and 19, 39°; 20, 39.1°; 21, 39°; 22, 38.7°; 23, 37.4°. The animal died during the night of the 23d. Its autopsy showed the characteristic lesions.

"It is necessary to push the temperature beyond 200° in order to destroy the toxic energy of the microbe, as we have seen its virulence resist simple ebullition. The microscope has shown that notwithstanding the boiling the micro-organisms retained their ordinary form *and continued to execute all of their movements*, a proof of their complete vitality" (*op. cit.* p. 217).

I may remark here that the micrococcus presented to me by Dr. Freire as his yellow-fever germ is killed by exposure for ten minutes to a temperature of 60° C. (140° Fahr.), and that it has no proper movements. Upon his return from Paris, Dr. Freire attempted to demonstrate to me the specific character of the micrococcus which he had presented to me, as his microbe of yellow fever, by a series of experiments upon guinea-pigs. He first proposed to "regenerate the virulence" of his cultures by passing the microbe through the body of a pigeon.

On the 7th July a bouillon culture was injected (1 gram) into the subcutaneous connective tissue beneath the wing of a pigeon. At the end of four hours the bird was killed, and 1 gram of blood from its heart was injected into the peritoneal cavity of a guinea-pig. The virulence of the microbe was supposed to be regenerated by its presence for the time mentioned in the blood of the pigeon. The question at once arose whether the micrococcus injected beneath the wing of the pigeon was really present in the circulation at the time the bird was killed. To test this, I mounted

* The thermal death-point of pathogenic micro-organisms. Am. J. of Med. Sci., July, 1887, pp. 146–160.

some blood from the heart for microscopical examination and made inoculations into three tubes of agar-agar. The result of the direct examination of specimens of blood stained with fuchsin was entirely negative, as was also that of the culture experiment. No development occurred in any of the agar tubes. On the 29th of July, twenty-two days after the experiment, the guinea-pig inoculated with blood from the heart of this pigeon still remained in good health. On the 9th of July, Dr. Freire inoculated two small birds, native of Brazil, with blood collected from the heart of the above-mentioned pigeon. I could not discover any micro-organisms in a stained (fuchsin) preparation of this blood.

July 13.—One of these little birds was found dead. Tubes of bouillon and of gelatine were inoculated with blood from its heart. In these I found, on the 19th, an abundant development of a minute bacillus resembling the bacillus of rabbit septicæmia. Dr. Freire insisted at first that the organism found in these cultures was identical with that—the micrococcus—which we had injected into the pigeon on the 7th of July. I pointed out to him the oval form, the end staining and the smaller dimensions, but was not able to convince him that the organism was not the same until I had made cultures in Esmarch tubes and demonstrated a difference in the appearance of the colonies and the fact that one organism—the micrococcus—liquefies gelatine and the other does not. The companion of the little bird which died in the above-mentioned experiment escaped from its cage on the 14th of July and flew away.

July 20.—Two guinea-pigs were inoculated with above-mentioned culture (from heart of small bird), one in cavity of abdomen, one in subcutaneous connective tissue. One of these guinea-pigs was found dead and one dying on the 30th of July. The one still living was killed, and two cultures were made with blood from its heart and liver in tubes of agar-agar. On the 1st August these cultures remained sterile; on the 4th August one of the tubes from the liver contained a bacillus with a single end spore, and one from the blood of heart a large coccus in tetrads. The other tubes remained sterile.

July 11.—Two guinea-pigs were inoculated in the cavity of the abdomen with about one gram each of a pure gelatine culture of Freire's micrococcus. One of these guinea-pigs was found dead on the morning of the 19th; the other died July 23.

Autopsy of No. 1.—Liver dark-colored and quite soft; spleen normal; no micro-organisms found in blood of heart on direct examination of specimens stained with fuchsin. Two agar-agar tubes inoculated with blood from heart. These remained sterile.

Autopsy No. 2.—Liver soft and dark-colored; spleen normal; bladder full of urine, non-albuminous; stomach empty; animal much emaciated; blood from heart used to inoculate one Esmarch tube and two agar tubes; no development in any of these tubes when examined at the end of five days.

Remarks.—Both of these guinea-pigs were supposed by Freire to have died of yellow fever, although they had been inoculated with a culture not "regenerated" by passing it through the blood of a pigeon, and one which he had taken with him to Paris and back. Yet he repeatedly asserts in his published works that the virulence of his microbe becomes quickly attenuated in cultures preserved for a short time. Thus he says in his address before the Dosimétrique Society of Paris, in 1887:

"Besides, the cultures become attenuated when left alone after a time by the influence of the air to such a degree that a liquid primitively virulent may be inoculated without danger seven to ten days after."

Notwithstanding the above very positive statement Dr. Freire was unwilling to show me his method of inoculating man by using some of this culture brought from Paris, and stated that the fact that these guinea-pigs had died was evidence that this culture—which had crossed the ocean and back—was too virulent to be used as a vaccine. Yet his experiments had been inaugurated with a view to regenerating the virulence of this same culture, upon the assumption that it was too attenuated to kill guinea-pigs.

On the 12th of July a second pigeon was inoculated with two grams of a gelatine culture of Freire's micrococcus; this was killed, as in the previous experiment, at the end of four hours and blood from its heart was injected into the peritoneal cavity of two guinea-pigs—one-half gram in each.

Two small birds, native to Brazil, and said by Freire to be very susceptible to yellow fever, were inoculated at the same time, by injecting a little blood into the muscles under the wing of each. These birds remained in good health so long as I had them under observation. On the 16th of July, four days after the inoculation, at the suggestion of Dr. Freire, one of the guinea-pigs, which remained in apparent good health, was killed by introducing a pointed instrument into the medulla. I examined a stained preparation of blood from the heart, but was not able to discover any micro-organisms in it. Two agar-agar tubes were inoculated with blood from the heart—they remained sterile.

The second of the above guinea-pigs died at the end of ten days, July 22. It was found dead in its cage at our morning visit on the date mentioned. Liver, dark-colored and soft; spleen, normal; bladder full of urine which is not albuminous. No micro-organisms found by me in stained preparations of blood from heart. Freire finds his coccus in these preparations. Two agar tubes inoculated with blood from heart remained sterile. One agar tube inoculated with pulp from interior of liver. This tube examined on Monday morning, July 25, was found to contain an abundant development of micrococci, which seemed to be identical with those in Freire's original culture. The tube, which I had sealed hermetically at the time of making the inoculation, had been opened by Dr. Freire for the purpose, as he said, of examining the culture. This culture was subsequently used for the following experiment.

Our guinea-pigs up to the present time had been kept in the animal room attached to Dr. Freire's laboratory, which had served for his former experiments, and contained a considerable number of wooden cages, some old and some new, which were arranged in rows, one above the other. I had originally purchased in the market twelve guinea-pigs, which were placed in these cages. As will be seen from the above account of our experiments, a number of these had died after various inoculations which we had practiced. But in the mean time I had several guinea-pigs in the same cages which, not having been inoculated, served as control animals—*témoins*. On the 14th of July, seven days after the guinea-pigs had been placed in these cages, the janitor of the laboratory reported that three of those not inoculated had already died. Dr. Freire suggested that they had probably died from yellow fever contracted in the laboratory, and stated that this had frequently occurred in his experience. Yet we were now in mid-winter, and no yellow-fever cases were to be found in the city. I naturally suspected that the cages in the animal room were infected with some micro-organism pathogenic for guinea-pigs, although none was found in my cultures. I therefore proposed that the next experiment should be made upon animals which had not been in the animal room, and which should be kept in a new cage in a room which had never been used for similar experiments. Accordingly the following experiment was made under these conditions:

July 25.—Inoculated two guinea-pigs in cavity of abdomen, with culture from liver of guinea-pig which died July 22. The guinea-pigs were placed in a clean cage in a closet attached to Dr. Freire's laboratory. At the date of my departure from Brazil, August 8, these guinea-pigs remained in good health. The fact that these animals did not die was accepted by Dr. Freire as evidence that the culture with which they were inoculated was sufficiently "attenuated," and he consented to make some inoculations in man in my presence.

DR. FREIRE'S METHOD OF MAKING PROTECTIVE INOCULATIONS.

In his address before the Dosimetrique Society of Paris, from which I quote as being one of his most recent statements, Dr. Freire says:

"The vaccinal liquid is prepared as follows: I inject the blood of a patient, dead,

or on the point of dying from yellow-fever, into the veins of a guinea-pig or rabbit; then the blood of this first animal is inoculated into the blood of a second of the same species, and thus in succession up to the sixth or seventh animal. With the blood of the last cultures are made, which are transplanted at least four times; it is then that I commence to inoculate man, not without having tested in advance upon animals if these inoculations were not capable of producing accidents of a certain gravity."

I would remark that all of the evidence heretofore presented goes to show that the micro-organisms present in Dr. Freire's cultures did not come from the blood of the yellow-fever patients from whom blood was taken, but from the surface of their bodies, or from accidental contamination with organisms floating in the air, etc.

He has simply shown by his experiments that such cultures during the summer months are pathogenic for guinea-pigs, but the inference that these guinea-pigs die of yellow fever has no scientific foundation. It is quite possible that in a locality where yellow fever is endemic, his cultures have at times contained the veritable yellow-fever germ, but if so we must regard its presence as accidental and unrecognized. With reference to the method of inoculation practiced, I quote from Dr. Freire's "Report upon preventive inoculations for yellow fever during the epidemic which prevailed in 1883 and 1884 in Rio de Janeiro."

"II.—*Method of preparing the cultures.*

"I have never inoculated in man blood or any other liquid taken directly from the cadaver or from one sick with yellow fever, as some persons have insidiously reported. I proceed in the following manner:

"I pass the blood of yellow-fever patients through an extended series of animals, into which I inoculate it successively, and it is the blood of these animals that I subject afterward to cultivation. After having transplanted the cultures more than four times I commence to inoculate them in man, after having previously verified upon animals if they are capable of producing accidents of a certain gravity.

"I make this observation in order that it may be seen that I have never proceeded lightly. It is evident that being thus prepared the cultures of the microbe which were inoculated in man represented a generation far removed from the primitive microbe, a tenth or twelfth generation which preserved its primitive characters of configuration and of development proper to the species, and which was characterized only by a notable diminution of the microbian energy.

"The attenuation is explained by the new *milieu*, in which I have placed the micro-organisms, in causing them to pass through the organisms of inferior animals and in cultivating them afterward in sterilized flasks containing beef bouillon, gelatine, or milk.

"It is proper to remark that in the epidemic intervals the cultures become attenuated, and the microbe feels the influence of the air in such a manner that if, in a sporadic case, we withdraw the blood of a patient and inoculate it some hours after into an animal, it happens very often that it is not attacked with the malady.

"It is for this reason that the sporadic cases are in general less grave than the epidemic cases; the sporadic microbe is already more or less attenuated by natural influences.

"I am happy to declare to your excellency that my method of attenuating cultures by transplantation from one species of animal to another species has been applied with success by M. Pasteur to modify the virus of hydrophobia by transporting it from the dog to the guinea-pig, the monkey, etc.

III.—*Method of vaccinating.*

"As was natural the timidity of my first efforts did not permit me to introduce into the human organism a large dose of the microbian culture. For this reason I have

employed in almost all the vaccinations the endemic method, and have only recently injected the same cultures into about twenty persons hypodermatically.*

"The cultures were withdrawn from Pasteur flasks with all the care necessary to avoid the entrance of foreign germs, and preserved in little flasks holding 4 to 8 grams, previously sterilized by heat and having ground glass stoppers. The liquid was poured into a clean watch glass and some drops taken upon the point of a vaccinating lancet and introduced under the skin by means of five or six punctures, leaving the point of the instrument inserted as long a time as possible, in order to assure absorption. The point chosen for practicing the inoculation was the deltoid region.

"When the hypodermatic method was employed about a gram of the liquor was drawn into a Pravaz syringe, and this was injected in the usual way.

"In future I shall give preference to the last-mentioned method as being more sure, since we have the certainty that all of the liquid employed goes to exercise its preservative influence."

Dr. Freire's vaccinations have been for the most part made by two apothecaries in Rio, who have acted under his instructions. The method in which the experiment was made as well as the theory upon which it was founded and the experiments which furnished the basis of this theory have all received severe criticism at the hands of some of the most prominent of Dr. Freire's confrères in Rio. As these criticisms have been published in the city of Rio, and are made by members of the Imperial Academy of Medicine, who enjoy the confidence of the Government and are now occupying important official positions, I think it proper to introduce them here. The following is a translation of a letter by the Baron de Ibiturnna, president of the central board of public hygiene, which was published in one of the daily newspapers of Rio:

YELLOW FEVER VACCINATION.

I am obliged to correct the statements made by Dr. Domingos José Freire in his article of the 7th instant, and in so doing I shall simply narrate facts, as I consider it unnecessary to enter into a formal discussion of the question.

On November 9, 1883, the department of the Empire gave the following instructions to Dr. Freire, then president of the board of health:

"As the board of health, at its meeting on the 16th ultimo, authorized inoculation with the liquid obtained from the culture of the microbe, for the purpose of testing its efficacy as a preservative from yellow fever, as you informed me in your communication of the 29th ultimo, you may insert advertisements in the Diario Official and in some other widely circulated journal, inviting, as you suggest, newly arrived persons or any others who desire to be inoculated to call at the Vaccine Institute on Wednesdays and Saturdays between 10 and 12 o'clock a. m. The cost of publishing the advertisements will be defrayed by this department.

"God guard you.

"FRANCISCO ANTUNES MAIREL.

"*To the President of the Central Board of Public Health:*"

When the sanitary service was reorganized, in virtue of the new regulations, I wrote to Dr. Freire inviting him to call at the board of health office on the days and at the hours mentioned in the above-quoted instructions for the purpose of continuing to perform inoculations with the microbian liquid, and in doing this I executed the orders of the minister of the Empire.

Dr. Freire, calling at the board of health office, informed me that he was ready to continue the yellow-fever vaccinations, but intimated that, as few persons went to the Vaccine Institute for the purpose of making use of his preservative, he desired permission to perform vaccinations in private houses when requested to do so.

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* "After being vaccinated nearly all the persons presented the following symptoms: Supra or infra-orbital cephalalgia; contusive pains along the vertebral column or in the limbs; elevation of temperature (from some tenths of a degree to a degree); general feeling of feebleness; sometimes the tongue was co ted; nausea and rarely vomiting; in some cases I have noted injection of the conjunctivæ. These phenomena have never compelled the person to keep his bed."

Exceeding my instructions, I gave him the authorization solicited and communicated the fact to the minister of the Empire, who approved of my action.

Some days afterwards I received information from health officers that some of Dr. Freire's vaccinators, calling themselves members of the board of health, and claiming to act under the authority of the police, were invading tenement houses and vaccinating by force every one they met without regard to race, color, nationality, time of residence in the country, or other circumstances which should be taken into consideration in the study of a scientific question of this importance.

I copy the communications received from the delegates of this board, so that M. Pasteur and other European *savants* may take note of our *savants* in this country who profess to keep pace with scientific progress and by certain newspapers are proclaimed compeers and rivals of the most brilliant ornaments of the scientific world.

"To His Excellency Baron de Ibituruna,
"*Inspector-General of Public Health:*

"I deem it my duty to inform your excellency of a serious abuse which should be promptly checked. Yesterday, when making a sanitary visit to Rua Conde d' Eu I was informed by a boy living in a tenement house on that street that the board had been there last week vaccinating the yellow fever. On my asking him who was the "board," he answered, Apothecary Telles.* He added that this vaccinator compelled the tenants to submit to the operation, threatening those who refused.

"Surprised at this statement, and indeed scarcely able to credit it, I asked the boy to show me some of the persons vaccinated by Mr. Telles, whereupon he conducted me to the tenement house No. 132 B and showed me several rooms whose tenants had been vaccinated.

"I was there informed by some poor ignorant Portuguese and negro women that Mr. Telles, accompanied by one of his clerks and another young man, had been there and commanded them all to be vaccinated with the microbe, such being, he said, the order of the Government.

"Some of them, intimidated, reluctantly submitted; others, more courageous, declared that they would not be vaccinated, no matter what might be the consequences. He ordered these to present themselves at the police office for having disobeyed the commands of the higher authorities.

"Growing angry and noisy, he commanded those who would not then be vaccinated to appear before the board as soon as possible, threatening the refractory with the police. One poor woman had to struggle to keep him from vaccinating her little child who was ill with fever and taking medicine.

"A negro woman showed me on her arm a hard knot, which she said was very painful, caused, as she declared, by the instrument which Mr. Telles used in vaccinating her.

"In the neighboring tenement house at No. 130 Mr. Telles also endeavored to vaccinate the tenants. He was resisted, however, by two Portuguese women, who declared that they would not submit to the operation, and that moreover they would not go before the police authorities, as they had not committed any crime.

"I deem it unnecessary to add to this statement anything to justify the indignation I felt when these facts were narrated to me or to prove that this abuse should be corrected. Mr. Telles is not even a pharmaceutist, and, even if he were a physician, he would not be allowed to inoculate with the yellow-fever microbe. Should he receive permission to do so, he assuredly would not be allowed to employ force, threats, and violence.

"I have deemed it my duty to communicate these facts to your excellency, who, I hope, will approve of my action in advising the tenants of these and other tenement houses not to allow Mr. Telles or any one else to vaccinate them except of their own free will.

"Dr. Dermeval da Fonceca.

"Rio, *March* 4, 1886."

"To His Excellency Baron de Ibituruna,
"*Inspector-General of Public Health:*

"In addition to what I yesterday made known to your excellency, I must inform you that I subsequently returned to the tenement houses on Rua do Conde d' Eu, having requested Dr. Aranjo Góes, member of the board of health, to be present for

* Apothecary Telles is a mulatto, who has a small drug store in a neighborhood surrounded by tenement courts (*corticos*). Four individuals were inoculated by him in my presence to demonstrate the method. One of these was a negro and another a Portuguese who had resided in Rio for many years. Telles informed me that he had inoculated more than two thousand individuals and that not only had the inoculation protected them from yellow fever but also from small-pox, which was prevailing as an epidemic at the time of my visit to Brazil.—G. M. S.

the purpose of taking the depositions of the tenants of those houses in regard to the abuses committed by the pharmacentist, J. Telles Sampaio.

"The following persons declared that Mr. Telles, by means of threats, succeeded in vaccinating them with the yellow-fever microbe:

"Porphyria, a negro woman residing in the tenement house at No. 130 B, Rua do Conde d'Eu.

"Amelia, a negro woman, twenty-three years old, living in the same house. She declares that in another room some of her children were also vaccinated by force.

"João Soares Guimães, a Portuguese. He declares that his wife was ordered by Mr. Telles to appear at the police office for having refused to be inoculated with the microbe.

"Maria Luiza da Silva, residing in the same house. She declares that Mr. Telles endeavored to vaccinate by force her little daughter, two years old, who was ill with fever. She stoutly opposed this, though threatened with the police.

"Emilia Augusta and Maria José, two Portuguese women, residing at No. 130 B, Rua do Conde d'Eu. They were ordered by Telles himself to appear at the police station for having refused to be vaccinated.

"Bernardino José Brito, a Portuguese, residing at No. 130 Rua do Conde d'Eu, and owner of a drinking saloon at No. 120 D of the same street. He declares that Mr. Telles, by force and fraud, vaccinated his six-year-old daughter against the wish of her relatives. The deponent was absent from home at the time, and, when on his return the fact was related to him, he was very indignant and wrote an article, which was published in the Gazeta de Noticias of January 23, complaining of the board of health, to which he attributed what had occurred, as Mr. Telles claimed to be a member of the board.

"The persons vaccinated say that Mr. Telles, when he went to the tenement-houses, carried with him the microbe in a cup, from which he took it with a large lancet. With this instrument he vaccinated on the arm the imprudent persons who had not the courage to resist his orders and threats.

"Communicating this to your excellency, I deem it my duty to add that many persons, supposing us to be emissaries of Telles, were afraid to give evidence or to show us any one who was willing to do so.

"Dr. Dermeval da Fonseca.

"Rio de Janeiro, *March* 5, 1886.

"A true copy.

"Dr. Pedro Affonso de Carvalho, *Secretary.*

"Board of Health, *March* 9, 1886.

"Board of Health, Lagôa District,
"*Rio de Janeiro, March* 20, 1886.

"To-day there appeared before us Mrs. Eliza de Jesus Alves, wife of Manuel Alves da Costa, jr., residing at No. 2 Rua de Sorocaba. She carried in her arms her little boy, some four or five years of age, whose body, head, and face were covered with a generalized ecthymic eruption. She declared that this eruption, which had appeared not only on the child she had brought with her, but also on four others, and on herself as well, had been caused by vaccinations (subcutaneous injections) performed, almost by force, on their arms by a man said to be an apothecary of the Rua do Conde, who said that it was to keep them from having yellow fever, and that for the poor this vaccination is obligatory. The operation was performed with incredible rapidity, almost without their consent, or that of other persons who were vaccinated at the same time, and even through shirt and coat sleeves. In view of such brutal conduct, we call the attention of the honorable board to these outrages, which are by no means the first cases of this kind, for complaints have been made by victims in other parishes. The poor child and his little brothers are in a really pitiable condition.

"Dr. Julis Branctao,
"Dr. Carneiro,
"*Delegates.*"

"To His Excellency Baron de Ibituruna:

"I wish to inform your excellency that I have caused to be disinfected the rooms in the tenement-house at Rua do Marquez de Abrantes No. 16, in which had died, of yellow fever, a boy named Carlos, three years of age, and son of Joaquim Pereira Tenas. This boy had been vaccinated with the culture of the yellow fever microbe by two persons who compelled him to submit to this operation.

"The obituary certificate was signed by Dr. Marinho de Azevedo.

"Dr. Azevedo,
"*Delegate for the Parish of Gloria.*

Rio, *April* 10, 1886."

In my interview with Dr. Freire, at the board of health office, I requested him not to continue to have vaccinations performed at the drug stores on Rua Primeiro de Marco and Rua de Conde d'Eu, refraining through delicacy and respect for his feelings from mentioning what I knew about the latter drug store, which is illegally under the direction of the practical druggist, Telles de Sampais, in virtue of verbal permission given by Dr. Freire, as president of the old board of health.

* * * * * * *

It is my sincere desire that Dr. Freire may continue to study the preservative action of his microbian cultures in relation to the yellow fever, but that he may do so calmly and without bias, like a scientific man, as did Edward Jenner in regard to vaccine matter as a preservative from small-pox.

Let him avail himself of the labors of his professional brethren, and let him select assistants qualified to elevate his theories in the opinion of the public and the profession instead of recruiting them among speculators and frequenters of tenement houses, who obtain greater numerical results by making victims and not disciples.

Let him again attend the meetings of the Academy of Medicine, where he has always been listened to with interest, and let him there recount his triumphs without showing offense if some colleague happens to differ from him. He should remember that science has always had its martyrs, but that these in compensation have been glorified by history.

Let him not be deceived by the praise bestowed on him in the press by persons who for purposes of their own make use of his name.

There have already been recorded many cases of deaths among persons inoculated with the microbian liquid, including the members of a respectable family vaccinated a year ago in Catumby. One member of this family died of a pernicious lymphatitis a few days after vaccination, and another of yellow fever a little over two months ago. Every one else in the house had the yellow fever, although vaccinated. The person who fared best, having only a mild attack, was one who was absent when Dr. Freire invaded the house and performed the vaccinations without the previous consent of the head of the family.

I am inclined to believe that Dr. Freire's failures would be fewer if the vaccinations had all been performed by himself; from those performed by force with the liquid carried about in a cup and with improper instruments by his assistants, who invade tenement-houses, science can expect little benefit and humanity still less. If Dr. Freire wishes, I will assist him in his meritorious labors. I will request the minister of the Empire to modify the instructions of November 9, 1883, so that Dr. Freire may be allowed to vaccinate in all the city and suburban parishes of Rio de Janiero, and I will appoint a delegate of this board to assist him and record his observations.

At the board of health office I myself will be his assistant.

I am sure that the minister of the Empire will not refuse to authorize me to have this done, for I have innumerable proofs of his sincere interest in everything relating to the improvement of the sanitary condition of the country.

Let Dr. Freire abandon his unfounded belief that everybody is opposed to him; let him fraternize with his professional brethren, whose praiseworthy scientific labors may be useful to him; let him close his ears to the flattery which fascinates him and causes him to deviate from the path he should follow, and his country and humanity will gratefully bless his name, if his efforts are crowned with the success we all so earnestly wish him.

BARON DE IBITURUNA.

RIO DE JANEIRO, *April* 11, 1886.

The following is from an address made by Dr. Nuno de Andrade, inspector-general of ports, at a meeting of the Imperial Academy of Medicine on the 14th of July, 1885. It is translated from the Bulletin of the Academy:

Dr. Freire says that the approach of the cool season is sufficient to neutralize the virulent force of the microbe and render it harmless, so that cultures which had previously been fatal to the animals inoculated were in cool weather entirely innocuous.

Dr. Freire still further remarks that not only the cultures but also the *very blood* taken from the corpses of persons who have died of yellow fever loses its virulence in cool weather, which he attributes to the microbes being dormant. All this is supremely obscure. It is not easy to understand how a microbe that has just killed a man can be considered dormant and unable to transmit the disease to a rabbit.

Besides, Dr. Freire, desirous of corroborating his assertion that the virus is spontaneously attenuated under the natural influence of the cool season, proceeded to make a number of experiments for the purpose of learning whether heat has the property of restoring to the microbe its virulence. These experiments are so con-

fused and unedifying that Dr. Freire, on page 242 of his new book, declares that "heat alone is not sufficient to restore to the microbe its venomous and deadly force."

Dr. Freire's doctrine in regard to the attenuating effects of the cool season seems, therefore, inexplicable. This, however, does not hinder him from saying on page 367: "After having proved by experiment that heat stimulates the virulent force of microbes * * * so that they produce venomous principles which occasion serious disorders and even death."

Dr. Freire's experiments *proved no such thing*, as he himself confesses on page 242, and, as he manifestly contradicts himself, there is no impropriety in asking which of the two opinions he definitely decides to adopt—that of page 242 or that of page 367?

If he adopts the former, he repudiates his attenuation theory; if he adopts the latter, the matter becomes more serious, and should attract the attention of the sanitary police.

In fact, Dr. Freire asserts that, owing to the recovery of their poisonous faculty by the cultures in summer, preventive inoculations should only be performed in the period from July to December (page 367). The speaker, therefore, invoked the just indignation of the president of the board of health upon the conduct of Dr. Freire, who, knowing that the cultures are noxious and even fatal in summer, is now inoculating with them in the tenement-houses of the city. Either the cultures have recovered their virulence, and in this case these inoculations are a calamity, or they are harmless, and in this case the doctrine of page 367 is false.

Dr. Freire's obscurities are so much the more to be regretted since that experimenter, shielding himself with the authority of the Imperial Government and the board of health, is inviting the public to be vaccinated, thus jeopardizing in an experiment of doubtful issue the dignity of the Government and the scientific circumspection of the board.

My instructions required me to investigate: "Second. The method of inoculation, which you will see verified if practicable on actual cases."

I showed my instructions to Dr. Freire, and mentioned my desire to see some inoculations made a day or two after first meeting him, but on the 23d of July, when I again urged this matter upon his attention, he stated that the culture brought from Paris was too virulent for such inoculations, as one of the guinea pigs inoculated with it had died. Yet, at the outset of our experiments, he had stated that it was necessary to regenerate the virulence of this same culture, which was from stock which he had taken to Paris with him, and must consequently have been obtained many months previously. Moreover we were now in the midst of the cold season in Rio, when, according to Dr. Freire's repeated assertions, neither blood nor cultures from it have any considerable virulence. He stated at this interview that it would be necessary to again attenuate the culture by injecting a quantity of blood from the heart of a guinea pig, just dead, into a pigeon, and from the pigeon into another guinea pig, and so on until one failed to die; the blood of the last could then be used to start fresh cultures, which would be suitable for inoculation. He would, however, inoculate two guinea pigs from the culture obtained from the liver of the guinea pig which died July 22, and if they did not die he would venture to use this culture. I did not ask him why some of the material in his numerous Pasteur flasks in the laboratory, which had served for the inoculation of so many persons in 1886, might not serve the same purpose at present, but I was at a loss to understand how it was that my witnessing a practical demonstration of his method was to depend upon the fact whether these two guinea pigs died or otherwise. As they remained in good health, arrangements were made by Dr. Freire to practice some inoculations in my presence, on the 8th of August, a few days before the time fixed for my return home.

The inoculations were made at the drug store of the apothecary Telles, who had made the greater number of his inoculations in 1885 and 1886. Dr. Freire brought with him the agar culture referred to, made in one of the tubes I had brought with me from Baltimore. About two grams of water was poured into the tube, and the micrococci upon the surface of the agar were mixed with this by stirring with a glass rod. One-half a gram of this water with the micrococci in suspension was then injected by means of a hypodermatic syringe in the deltoid region of the arm of each of the individuals selected for the experiment.

These persons were:

(1) Pedro Bernard de Senna; a negro; aged twenty-nine years; a native of Brazil; residence Rua Misericordia No. 52. This man was under the influence of liquor when inoculated. He did return, as he promised to do, to let me see his arm on the second day after the inoculation.

(2) José Francisco da Sieva Ramos; aged thirty-four years; born in Portugal; has been twenty-five years in Brazil; residence 87 Conde d'Eu; occupation upholsterer. This man reported to me at the drug store the second day after the inoculation. His temperature was 98.°4 Fah.; some tumefaction, redness, and pain on pressure at point of inoculation; says he had a little headache the night before.

(3) José Candido da Souzá; aged twenty-six years; Portuguese; five months in Brazil; a baker. Not vaccinated before, and has not had yellow fever. This man returned for examination on the 10th. There was tumefaction, redness, and pain on pressure at point of inoculation. Temperature 98.3° Fahr.; no chill and no fever; says he had a little headache and malaise, but has continued at his work.

(4) Serafim Francisco dos Santos; Portnguese; aged eighteen years; four years in Brazil; a baker. Not vaccinated before, and has not had yellow fever. On reporting two days later his temperature was found to be normal. There was slight tumefaction, redness, and pain on pressure at point of inoculation; has continued at his work, and has not had any symptoms as a result of the operation except a slight headache.

As I sailed for the United States on the 11th, I was not able to see these men again, but at my request Dr. R. Cleary, an American physician practicing in Rio, witnessed the inoculations and visited the two bakers after my departure. Since my return I have received the following letter from Dr. Cleary:

RIO DE JANEIRO, *August* 13, 1887.

DEAR SIR: I have just returned from a visit to No. 93 Rua do Conde d'Eu to examine the two bakers, Serafim Francisco dos Santos and José Candido da Souza, who were inoculated by Dr. Domingos Freire in our presence in the apothecary shop No. 87, in the same street. The swelling at the place of puncture has entirely subsided in one of them, and almost so in the other. It is still a little hard for about the size of a dime, and slightly discolored, very slightly (extravasated blood). The temperature of the inoculated places, as well as that of the whole body, is in a normal state, as well as the tongue, pulse, and skin; in fact, they appear in perfect health. Also, he felt no pain from pressure on the place.

I am, very respectfully, your obedient servant,

R. CLEARY.

August 16, 1887.—I have again seen the bakers to-day. No more signs of the inoculation appear. They are well, and no abscess formed.

R. C.

Dr. G. M. STERNBERG, *U. S. Army.*

Since receiving the above letter I have again heard from Dr. Cleary, and quote as follows from his letter, dated January 14:

Some days ago I met in the Rua Ouvidor the apothecary at whose shop Dr. Freire made the inoculations in our presence, and he reiterated his great faith in the discovery, and that it protected from variola also. A few days afterward the authorities closed this shop as an illegal concern.

DR. FREIRE'S PROTECTIVE INOCULATIONS.

Having reviewed at length the claim of Dr. Domingos Freire to have discovered a specific yellow fever germ, and to have transmitted this disease to certain lower animals by inoculation, and having arrived at the conclusion that these claims are without scientific foundation, it may be thought that no further demonstration is required in order to show that his protective inoculations are without value. The inoculations practiced are said to have been made with cultures containing the "attenuated" microbe of yellow fever; *a priori* it would appear that if there has been no veritable discovery, and if there is no sufficient evidence that the cultures used in

making the inoculations contained the specific germ of yellow fever no value can be attached to such inoculations.

But these inoculations have been made on so large a scale, and the statistical results, as presented by Dr. Freire in his numerous publications, appear so favorable to his method that it becomes necessary to analyze these statistics; and if, as he claims, they establish the fact that the mortality from yellow fever is very much less among those who have been inoculated by him than among non-inoculated persons exposed in the same way, we will be obliged to concede the value of his method, although the rationale of this protective influence may not be apparent.

Dr. Freire has given in detail his statistics relating to his yellow fever inoculations in the following publications, which we will consider separately:

I. Rapport sur les inoculations préventives de la fièvre jaune durant l'épidémie qui a régné en 1883 et 1884, à Rio de Janeiro et présenté à S. Ex. M. le Conseiller, ministre et secrétaire d'Etat de l'Empire, par le Dr. Domingos José Freire, professeur de chimie organique et biologique de la Faculté de Medecine de Rio de Janeiro, president de la Junte Centrale d'Hygiene, etc. (Rio de Janeiro, 1885).

II. Le vaccin de la fièvre jaune. Résultats statistiques des inoculations préventives pratiquées avec la culture du microbe atténné, de janvier à août de 1885. (Rio de Janeiro, 1886).

III. Statistique des vaccinations pratiquées avec la culture attenuée du microbe de la fièvre jaune de Septembre, 1885 à Septembre, 1886. (Paris, 1887.)

In order to do full justice to Dr. Freire I shall quote extensively from these several reports. I will then state the results of my own investigations and will make such an analysis of the statistical data given as seems to me necessary in order to elucidate the truth with reference to the question as to the real value of the inoculations practiced as a protection against yellow fever.

REPORT UPON PREVENTIVE INOCULATIONS FOR YELLOW FEVER DURING THE EPIDEMIC WHICH PREVAILED IN 1883 AND 1884 IN RIO DE JANEIRO.

[Presented to his excellency the minister, councillor, and secretary of state of the Empire by Dr. Domingos José Freire, professor of organic and biologic chemistry of the faculty of medicine of Rio de Janeiro, president of the central board of health, etc.]

EXCELLENCY: The epidemic cycle of yellow fever which commenced to manifest itself in the month of October of the past year having terminated, as only sporadic cases show themselves at the present moment, I consider it my duty, having been commissioned by the Imperial Government to study this malady, to communicate to your excellency in a succinct manner the practical results of the researches which I have made since March 15, 1883, the date upon which I was charged with this task, which has been as arduous as it is flattering for me, by M. the Councillor Leão Velloso, minister of the Empire at that time.

Before occupying myself with all of the details relating to this question in the work entitled "Doctrine microbienne de la fièvre jaune," already in course of publication by order of the Imperial Government, I will limit myself at present to submitting to your excellency the labors which relate to the problem of preventive inoculations, the capital point and final end towards which the studies which I have undertaken have tended from the commencement.

I will make in brief chapters an exposition of the fundamental facts which have brought me to test upon the human species this means of prophylaxis and the results of this first experiment, which can already be appreciated upon a grand scale, inasmuch as the vaccinations were no sooner practiced than an epidemic of yellow fever occurred, which has carried off nearly seven hundred victims.

Basis for vaccination.

It was only after long and patient experiments upon the virulent power of the microbe of yellow fever that I was encouraged to inoculate in the human organism. I have realized from the commencement the immense responsibility which would weigh upon my conscience in case a single disaster should come to reduce to nothing the series of my deductions. I can assure your excellency that in this grave question I have proceeded with all the precaution, all the care, all the prudence required in such a case, and the proof is that up to the present time I have not had to repent of a single one of my acts tending to elucidate the problem of the prophylaxis of yellow fever, in spite of the intrigues of my adversaries and of the sad expedients to which they have resorted to satisfy their animosity against me.

I could, however, fear nothing, because I have founded my experiments upon the most certain basis of physiological experimentation and comparative pathology, and I have repeated the facts a great number of times and under the most varied forms of intensity and of animal organization.

In the first place I occupied myself in verifying the contagious nature of the malady, which I have put beyond doubt by means of inoculations of the blood of individuals attacked with yellow fever into susceptible animals; I transmitted the malady from animal to animal in the same way as in its natural evolution it is transmitted from man to man, a result which I have related in a little brochure entitled "Études expérimentales sur la contagion de la fièvre jaune."

After having demonstrated the contagion not only by these inoculations, but likewise by the cadaveric examination of animals which presented lesions in every respect similar to those encountered in man, I occupied myself in seeking a proceeding for the attenuation of the microbian virus, and I remarked that after a certain number of successive cultures made with all scientific rigor the microbe lost a great part of its virulent activity and could be inoculated into the same susceptible animals which had served to demonstrate the contagious nature of the malady without producing death.

In effect, guinea-pigs which all died under the influence of direct inoculations of blood and of very virulent cultures, resisted the attenuated cultures even when they received by injection 50 centigrams or a gram at once. These animals presented only a slight elevation of temperature and loss of flesh, and other symptoms which passed away in two or three days, after which they returned to their normal condition. There exist still in my laboratory several animals inoculated more than a year ago, the health of which has not suffered.

This remarkable attenuation of the cultures has struck me so forcibly that I occupied myself immediately in ascertaining if the animals inoculated with these cultures gained, or otherwise, an immunity when injected with virulent blood drawn from individuals affected with yellow fever.

In twelve animals vaccinated several days previously with attenuated cultures, the injection of this blood did not produce death, while in other animals, not vaccinated, in which the same injection was made at the same time, death occurred in all. I am making preparations to repeat my experiments upon a greater scale during the next epidemic, in view of the fact that I have no longer any cultures which have a mortal virulence.

These twelve cases have, however, a great value for me, and as I had demonstrated physiologically in more than fifty experiments upon animals, the innocuity of the attenuated cultures, I had a foundation sufficiently secure to make me feel authorized to test upon the human species preventive inoculations with the same cultures.

Number of persons vaccinated and conditions in which they were placed.

I have practiced four hundred and eighteen vaccinations upon the human species, not only a month before the epidemic, but also during the period of its greatest intensity.

Experience has demonstrated that the most favorable conditions for being attacked and dying from yellow fever are:

(1) Absence of acclimation. It is for this reason that strangers recently arrived are most subject to be attacked, as well as natives coming from places where the disease does not reign habitually.

(2) An age comprised: (*a*) between sixteen and thirty years (maximum of frequency); (*b*) between thirty-one and forty-five years; (*c*) between less than one year and fifteen years. From forty-five to sixty the disease is more rare, and after sixty it is excessively rare.

(3) A strong constitution, which corresponds with the limits of age already stated.

(4) Bad hygienic conditions, above all the agglomeration of persons offering these conditions of receptivity in non-hygienic habitations.

I have sought to vaccinate only individuals included in these conditions of morbid receptivity. The four hundred and eighteen persons vaccinated may be classified as follows:

First. Age.—From sixteen to thirty years, 241 (maximum intensity); from thirty-one to forty-five years, 94 (intermediate intensity); from less than one year to fifteen years, 64 (intermediate intensity); from forty-six to sixty years, 13 (minimum intensity); without declaration of age, 6; total, 418.

Second. Nationality.—Portuguese, 158; Italians, 122; French, 11; Spanish, 9; English, 1; German, 1; Swiss, 1; North American, 1; Argentine, 1; Holland, 1; Pole, 1; Brazilians, 111.

Important observation.—The 111 Brazilians came, with rare exceptions, from the high plateaus (interior of the Province of Rio de Janeiro) or from the provinces of the south, from Minas, Geraes, San Paulo; a few from the provinces of the north. They were then all in the most favorable conditions of morbid receptivity.

Third. Time in Brazil.—A few days, 39; from one month to one year, 166; from two to five years, 114; more than five years, 26; total, 345.

There are seventy-three persons for whom no statement is made as to time of residence in Brazil, but in this number is included many children of a few months or years of age.

The greater number of those vaccinated inhabited the *estalagens** and lived in the quarters where the disease habitually prevails with the greatest virulence; that is to say, at Cidade Nova, in the center of commerce, and the littoral from the beach of Santa Lucia as far as Botafogo, throughout its extent and in its vicinity.

I vaccinated in Vassouras thirty-seven persons; but these persons had to visit Rio during the epidemic season, and for this reason desired to protect themselves. Besides, it is known that recently deadly epidemics of yellow fever have broken out at Vassouras, and it appears that several sporadic cases have already occurred this year. For this reason I could not and ought not to neglect as a statistical element the vaccinations made at Vassouras.

Result of the vaccinations.

During the epidemic season a great number of those vaccinated were attacked by the disease, but in a manner quite benign. At the termination of the epidemic we have ascertained that up to the time of presenting this report more than six hundred and fifty persons not vaccinated have died of yellow fever. On the other hand, seven persons *among the vaccinated* appear in the lists of deaths as having died of the malady, and even of these there are well-founded doubts as to the correctness of the diagnosis in different cases; for this reason I ought to call your excellency's attention to the fact that I have only been able to verify the diagnosis in two of these cases.

Let us admit, however, that the number of deaths has been seven; even then the percentage of deaths will be very favorable since it will be scarcely 1.6 per cent.

* * * * * * *

This statement of results is followed by a further discussion of the ages and nationality of those vaccinated, and a comparison with the ages and nationality of those included in the list of deaths. Following this is a list of the names of the vaccinated, in which is included a statement of the age, nationality, residence, and time of residence in Brazil. This is followed by a list of the names of those who died from yellow fever in Rio de Janeiro between the months of October and May, 1884. In this list, also, the name, nationality, and residence is given.

We remark, first, that, in selecting foreigners, and, preferably, those who had recently arrived in Brazil, for his first experimental test as to the efficacy of his protective inoculations, Dr. Freire has given evidence of his confidence in the method of prophylaxis proposed, and of an honest desire to demonstrate its value, and nothing could be more fair than his full publication of the names and of the essential facts with reference to these persons. I must object, however, to his including in his statistics the names of thirty-seven persons residing in Vassouras, a village which is some 50 miles distant from Rio de Janeiro. Even if these persons had occasion to visit Rio during the epidemic season, as is stated by Dr. Freire, it is probable that they would remain as short a time as possible, and there is no evidence that they were fairly exposed to the epidemic influence. Moreover, if any of these persons had contracted yellow fever as a result of a visit to Rio, their names would not appear in the mortality lists of this city, but in those of Vassouras, which are not given. The latter objection applies also to fourteen persons among the vaccinated whose place of residence is Nictheroy, a town upon the Bay of Rio de Janeiro, which is the capital of the province of the same name; two persons vaccinated at Tijuca and one on board the bark *Flive*, two at Pavina and three at Serraria, must also be excluded. This reduces the number of vaccinated persons within the city limits to three hundred and fifty nine; and, of this number, a certain proportion, no doubt, left the city soon after being vaccinated, and before any exposure worthy of consideration in a test of this kind had occurred.

Dr. Freire admits that, "during the epidemic season, a great number of the vaccinated were attacked by the malady;" but claims that these attacks were of a mild

* Small apartments where the laborers, and especially those of foreign origin, are crowded together.

character; yet he gives us the names of seven vaccinated persons who died from the disease. This list has been added to by some of Dr. Freire's confrères, as will be seen by the following translation of a letter published in one of the newspapers of Rio, and bearing date May 5, 1887. This letter is signed by Dr. Aranjo Góes, at present a member of the central board of health, and a gentleman whose statements are worthy of the fullest confidence.

My letter to the Imperial Academy of Medicine having been published, it now behooves me to publish the statistics relating to the vaccinations on Morro da Vinva.

One fact seems to me to be definitely demonstrated, that is the *worthlessness of Dr. Freire's vaccination*, as is well known to the medical profession of this city.

A year ago I wrote the following:

"The want of skill which he displayed in his first experiments, the false conclusions which he has drawn therefrom, and the thoughtless precipitation with which he has hastened to make known incomplete results without accompanying them with a single qualifying remark vitiate all the methods to which he may hereafter resort to corroborate his statements." (Jornal do Commercio, April 20, 1883.)

The mortality among the persons vaccinated on Morro da Vinva furnishes one more proof that I was right in saying this, as I now proceed to demonstrate.

There were vaccinated in this district sixty persons. Sixteen removed shortly after the commencement of the epidemic, and forty-four remained exposed to its influence. Of these twenty-two had the yellow fever, nine of whom died.

The following is a list of the vaccinated persons who had the fever, the names of those who died being marked with an asterisk:

Antonio de Oliveira,* Antonio Bento da Silva, Albino Francisco Maia, José da Silva, Joaquim Pereira de Souza,* Joaquim Gomes de Azevedo, Joaquim Ferreira Tollio, José Seabra dos Santos, José Ventura, José de Souza Ferreira,* José Gomes de Azevedo, jr., José Farinha, Manoel Joaquim Pereira Lopes, Manoel Gomes de Azevedo, Manoel Antonio,* Seraphim Gonçalves Raymundo, Manoel Simões,* Thomé Simões, Manoel da Silva Alves,* Antonio Pereira Neves,* Joaquim Martins Pinheiro,* Joaquim Antonio dos Santos Cardoso.*

Consequently, of the forty-four vaccinated persons who remained in the locality, twenty-two, that is 50 per cent., had the yellow fever.

Of the twenty-two patients nine died, that is 40.9 per cent.

In the Jurujuba Hospital, which receives scores of patients already dying or in the third stage of the disease, the mortality is only 21 per cent.

It may also be of some interest to the English admiralty which, through ignorance or inhumanity, is very backward in publishing the translation of Dr. Freire's pamphlet.

Seriously, of what use is this vaccination? It serves to discredit in foreign countries the science and even the good sense of the Brazilians.

The competent, the veterans of microscopic investigation, who after two or three years of daily labor only dare in matters of this kind to give modest utterance to a simple hope, can not refrain from smiling at the achievements of Brazilian *sages*, who after two or three months' study solve the most difficult etiological and prophylactic problems relating to the most complicated diseases.

Since the mortuary statistics of the Morro da Vinva have been made known, his excellency, the minister of the Empire, and the honorable board of health can no longer cover with the mantle of their authority the repeated announcements enticing the ignorant and imprudent to be vaccinated with the microbian liquid.

Let the Morro da Viuva be the Waterloo of Dr. Freire alone.

Dr. Aranjo Góes.

May 5, 1884.

Upon comparing the names given by Dr. Góes with those in Dr. Freire's published list of persons vaccinated, I fail to find the following names: Joaquim Pereira de Souza,* Joaquim Gomez de Azevedo, Manoel Gomes de Azevedo, Manoel Simões,* Manuel da Silva Alves, Antonio Pereira Neves.*

On the other hand, Dr. Freire gives the name of Thome Simões as having died, while his name appears in Dr. Góes list without the asterisk, which designates a fatal case. Again Dr. Freire gives the name Celestina Felitte as one of the fatal cases conceded by him, but I do not find this name in his list of persons vaccinated.

In a second letter published in the Gazeta de Noticias (May 8, 1884), Dr. Góes criticises Dr. Freire's statistics as follows:

* * * * * * *

Ever since Dr. Freire, with such boldness and precipitation, spread to the four points of the compass the news of his famous discovery of vaccination for the preven-

tion of yellow fever, all of his professional brethren, even the most incompetent, have been entitled to investigate and criticise his experiments and theories, and it is his place to answer all objections which may be raised. To ask the public to suspend its decision, to postpone the refutation of the arguments against him, to equivocate, and to alter facts to suit his purposes, all this is a sign of weakness and a tacit confession of defeat.

The vaccination question may be divided into two parts, the first relating to the percentage of vaccinated persons attacked by the fever, and the second to the mortality among those attacked. Dr. Freire, being unable to deny that of forty-four persons vaccinated on Morro da Viuva twenty-two had the yellow fever, resorts to a subterfuge. He embraces in his statistics all who were vaccinated with the microbian liquid, whereas he should have included only those exposed to the influence of the epidemic.

For instance, of the sixty persons vaccinated on Morro da Vinva sixteen removed to other localities.

Dr. Freire does not deduct from the whole number the fifty or sixty persons vaccinated in Vassouras. He makes no deduction of Brazilians or foreigners who have long resided in the country. Neither does he deduct persons who have left the city and gone to Minas, St. Paulo, etc. He considers the whole number as four hundred and fifty, and thus arrives at a death-rate of 2 per cent. It is evident, then, that it is Dr. Freire that vitiates the calculation, including therein vaccinated persons absent from the city, and consequently out of reach of the epidemic.

This mode of reasoning does not indicate scientific candor, and it deserves the severest censure. The death-rate of 2 per cent. is altogether fictitious.

* * * * * * *

As long as Dr. Freire is unable to dispute my figures, he is forced to acknowledge the correctness of my conclusion that his vaccination is good for nothing.

Dr. Aranjo Góes.

May 7, 1884.

Dr. Freire's statistics have also been severely criticised in the Imperial Academy of Medicine of Brazil, as will be seen by the following translation of an address made by Dr. Nuno de Andrade, inspector-general of hygiene of the ports of Brazil.

The translation is from the published bulletin of the academy, and the address was made at the meeting of July 14, 1885:

In the second part of the order of the day the question discussed was yellow fever. Dr. Nuno de Andrade, taking the floor, said that there was not sufficient time for a thorough discussion of the question of Dr. Freire's inoculations for the prevention of yellow fever, and it was necessary for the academy to hear different opinions and not alone those of the speaker who had already, at previous meetings, occupied its attention. He would, therefore, make his remarks as concise as possible.

* * * * * * *

But, passing over all these incidents, the speaker proceeded to explain to the academy Dr. Freire's singular method of arranging statistics to prove the efficacy of his preventive inoculations.

To impress the Government with the idea that these inoculations had produced a wonderful effect, Dr. Freire sent to the department of the Empire a nominal list of the persons he had vaccinated and also a list of the deaths caused by yellow fever in this city in 1884. On examining these lists, says Dr. Freire, it will be seen that of the four hundred and eighteen persons vaccinated only seven, whose names he gives, have died.

The speaker said that he felt at a loss to estimate correctly the value of these lists. In the first place the list sent to the Government differs from that which Dr. Freire sent to the Gazeta de Noticias. Dr. Freire vaccinated four hundred and eighteen persons, but the list sent to the Government contains only four hundred and fourteen names. The names wanting to complete the number of four hundred and eighteen, were those of Antonio Gonçalves Martins, Camillo Lange, Felicio Rogeri, and Victor Sanzenzi. But it was likewise to be noted that Dr. Freire, having vaccinated fifty-nine Portuguese on Morro da Vinva, as may be seen by the list sent to the Gazeta, included in the list sent to the Government the names of only forty-nine. Consequently he had failed to account for ten, whose names are as follows: Braz da Silva Souto, Joaquim Gomes, Joaquim Gomes de Azevedo, José Pereira Lessa, Joãs Ferreira Vianna, José Monteiro dos Santos, Manoel Raymundo, Manoel Gomes de Azevedo, Manoel Ferreira, Seraphim Ferreira.

Including these ten, the number of persons vaccinated would be four hundred and twenty-eight; but as Dr. Freire only vaccinated four hundred and eighteen, it is to be supposed that the ten names omitted were replaced by ten others. These the speaker would give afterwards.

One of the ten vaccinated persons whose names had been overlooked when the list was prepared for the Government, the Portuguese Manoel Ferreira, twenty-three years old, residing on Morro da Viuva, died of yellow fever, as may be seen in the obituary list. It is necessary, therefore, to add this death to the seven given by Dr. Freire, and also that of Joaquim Antonio Cardoso and that of José de Souza Ferreira, making ten altogether.

It is impossible to say, with certainty, whether those ten are the only ones who died, for in Dr. Freire's lists some of the names are altered and do not agree with those in the obituary list.

For instance, the last-mentioned name, that of José de Souza Ferriera, was included in the list of persons vaccinated, together with a description of the person to whom it belonged, whereas, in the obituary list sent by Dr. Freire to the Government, while the description remains unchanged, the name is altered to José de Souza *Fonseca*. Examining the obituary lists published in the daily papers, the speaker found in the Jornal do Commercio, of April 5, 1884, among the deaths of March 31, that of José de Sonza *Ferreira*, just as it is in the list of vaccinated persons, and not *Fonseca* as it is in the obituary list which Dr. Freire sent to the Government.

The speaker said that he mentioned these facts not only to justify his own doubts, but also to show how carelessly Dr. Freire had done his work. The process of manufacturing statistics discovered by Dr. Freire exceeded anything the speaker had ever deemed possible, for his statistics for Rio de Janeiro in 1884 were prepared with data obtained in Senegal in 1881. What Dr. Freire proposed to ascertain was whether in 1884 the number of deaths in Rio de Janeiro, in proportion to that of the persons liable to take the yellow fever, was greater or not than that of the deaths among vaccinated persons in proportion to the whole number vaccinated. With this object in view he said: "In Senegal, in 1881, of four foreigners with less than three years' residence in the country three had the yellow fever, and of these two died; therefore the proportion of cases of yellow fever was 75 per cent., and the mortality among the patients was 66.6 per cent. In Rio the mortality in 1884 was 35 per cent."; *ergo*, reasoned Dr. Freire, 35 (of Rio): 66.6 (of Senegal) : : x (of Rio): 75 (of Senegal). In this calculation, whose wonderful ingenuity had greatly impressed the speaker, $x = 39.4$. "Thus," concluded Dr. Freire, "in Rio de Janeiro, in 1884, of every 100 persons liable to have the yellow fever 39.4 were actually taken with it; and as the mortality was 35 per cent., represented by 654 deaths, the whole number of patients was 1,873." Wishing to learn next how many persons there were in Rio, in 1884, liable to have the yellow fever, Dr. Freire established the following proportion:

$$39.4 : 100 : : 1873 : x.$$

Therefore $39.4\,x = 187{,}300$, and $x = 4{,}737$. Hence Dr. Freire concludes that in 1884 there were in Rio de Janeiro only 4,737 persons liable to have the yellow fever, and that of these 654, or 13.7 per cent., died, while of the 418 vaccinated there died only 7, or 1.6 per cent.

From this he infers that the result of his preventive vaccinations is really wonderful. (Page 181 of "Appendix to the Doctrine Microbienne.")

The speaker, however, preferred omitting the statistics of Senegal and making use only of those of Rio. Deducting, then, from Dr. Freire's list of vaccinated persons those who had more than three years' residence, and those residing in Vassouras and Serraria, the number of those liable to have the fever, according to the theory advanced in Dr. Freire's calculation, is reduced to three hundred and forty. Among these there were ten deaths, *i. e.*, a mortality of 2.9 per cent.

The number of foreigners who arrived in Rio de Janeiro in 1880, 1881, and 1882 was 66,628, all liable, according to the aforesaid theory, to have the fever.

This number, which is taken as a basis for the calculation, said the speaker, is not exaggerated, for if it be true that many of these persons did not remain in the city, it is also true that the calculation does not include the tens of thousands of sailors on board the vessels in port, nor the persons newly arrived from the country, nor the children residing here, who are unfortunately paying a heavy tribute to the epidemic.

Very well, the 654 deaths from yellow fever among the 66,210 persons liable to take the disease (66,628—418 vaccinated by Dr. Freire) represent a mortality of 1.01 per cent, which is much smaller than the mortality among the vaccinated.

At this point the speaker said that owing to his fatigue and to the lateness of the hour he would, for the time, terminate his address.

Upon my arrival in Rio I determined to make an attempt to ascertain the results, up to date, of the inoculations practiced by Dr. Freire in 1884, and included in the list published in his report at present under consideration. For this purpose I secured the services of Mr. Slaughter, a native of the United States, who has resided in Brazil more than twenty years, and has become a naturalized citizen of that country. I instructed Mr. Slaughter to visit each address in the published list, for the purpose of

making inquiries with reference to the vaccinated person and ascertaining, if possible, whether he had suffered an attack of yellow fever subsequently to the date of his vaccination.

The general result of this investigation is as follows:

Total number of vaccinated persons in Dr. Freire's list		414
Did not reside in Rio at time of vaccination	59	
Full address not given, and no visit made in consequence of this fact	82	
Not visited because of remoteness of dwelling and insufficient time	76	
Visit made to address given and no information obtained	111	
		328
Remaining		86

Of those remaining, information was obtained as follows:

Continue to reside in Rio and have not suffered from yellow fever since vaccination	30
Have suffered non-fatal attacks of yellow fever*	15
Have suffered fatal attacks of yellow fever*	10
Have removed from Rio, and did not suffer an attack, so far as could be ascertained before removal	23
Have removed from Rio, and are said to have suffered an attack of yellow fever since vaccination	3
Have died since vaccination: Of consumption, one; died after four days' illness, informant does not know cause of death or name of attending physician (No. 143); died December 29, 1883, one or two months after vaccination, informant does not know the cause of death (No. 410); is said to have died, no further information obtained (No. 349); total	4
Had yellow fever before vaccination	1

In addition to the ten fatal cases of vaccinated person included in the above list, Dr. Freire reports the name of Celestina Felitte, which does not appear in his published list, and Dr. Goes the names of Joaquim Pereira de Souza, Manoel Simões, Manoel da Silva Alves, and Antonio Pereira Neves.

The evidence above recorded seems to the writer to be convincing as to the complete failure of Dr. Freire's proposed method of prophylaxis as practiced in 1883 and in 1884. We can not, however, leave the question here, inasmuch as a modification of the method was adopted in 1884 and a large number of persons have been since inoculated by this modified method. Dr. Freire says in his report under consideration: "I have employed in nearly all of the vaccinations the endermic method, and it is only recently that I have injected into two persons the same cultures by the hypodermatic method." * * * "I shall hereafter give the preference to the last-mentioned method, because one is more sure that the liquid employed goes to exercise its preservative influence."

STATISTICAL TABLES OF THE INOCULATIONS PRACTICED FROM JANUARY TO AUGUST, 1885 (CITY OF RIO DE JANEIRO).

I. Nationality.

Brazilians	2,186	Foreigners:	
Foreigners:		Austrians	2
Portuguese	640	Greek	1
Italians	124	Paraguayans	20
Spaniards	22	Africans	4
French	14	North Americans	5
English	9	Chinese	2
Belgians		Hollander	1
Germans	2		

* The names given by Dr. Góes of cases occurring among vaccinated persons on Morro da Viuva are included; also the fatal cases reported by Dr. Freire.

Among the 2,186 Brazilians are included about forty negroes and mulattos.

Observations.—Total vaccinated, 3,051, viz, 2,186 natives and 865 foreigners. Among the natives are included 625 sons of foreigners of low age and having the two conditions of receptivity, which place them almost upon the same level with foreigners. A great number of the natives came from distant provinces, the climate of which is more temperate. They all inhabited the quarters infected by yellow fever.

The children of foreigners are of the following parentage:

II. Children.

Portuguese	545	French	3
Spaniards	9		
Italians	49	Total	625
Germans	19		

III. Ages.

Below 10 years	1,697	From 51 to 60 years	41
From 11 to 20 years	585	Over 60 years	4
From 21 to 30 years	348	Unknown	1
From 31 to 40 years	238		
From 41 to 50 years	137	Total	3,051

Observation.—It will be seen that the great majority of the persons vaccinated are within the limits of age most inclined to yellow fever. There are included a very considerable number of young children.

IV. Time of residence in Brazil.

A few days	26	Five years	103
A few months	71	On board ship (de passage)	9
From one year to a year and a half	69	More than five years	256
Two years	107		
Three years	98	Total	865
Four years	126		

Observations.—The nine individuals on board ship remained a long time exposed to the epidemic influence. Among the two hundred and fifty-six strangers who had remained more than five years we count a considerable number who have arrived in Brazil within six or seven years, that is to say, within the limits when they are still very susceptible. Besides, immunity is never absolute as a result of long residence in an infected country. Thus the individuals who are in this category afford each year a contingent, small, it is true, to the general mortality.

STATEMENT OF HOUSES AND STREETS WHERE DEATHS OCCURRED FROM YELLOW FEVER AND IN WHICH INOCULATIONS WERE PRACTICED THE DAY THE DEATH OCCURRED OR A FEW DAYS BEFORE OR AFTER.

1. *Rua de Riachuelo.*

No. 205.	Vaccinations	5
	Died not vaccinated	1
No. 39.	Vaccinations	35
	Died not vaccinated	2
No. 43.	Vaccinations	19
	Died not vaccinated	1
	Vaccinated in the adjoining house, No. 45	1
No. 199.	Vaccinations	3
No. 188.	Vaccinations	1
No. 172.	Vaccinations	2
No. 189.	Dead not vaccinated	1
No. 192.	Dead not vaccinated	1
No. 195.	Dead not vaccinated	1
No. 119.	Vaccinations	12
No. 114.	Dead not vaccinated	1

Vaccinations were also practiced at Nos. 274 (1), 260 (2), and 3 (5).

En résumé.—Vaccinations practiced in Rua Riachuelo, 114; died not vaccinated, 15. We have only mentioned those vaccinated who resided in the vicinity of individuals who died or in the same house. The same method will be followed for the other streets. Sixteen cortiços in this street.

2. *Rua de Comte d'Eu.*

No. 79. Died not vaccinated 1
No. 97. Died not vaccinated 1

In Nos. 87, 93, 85, 91, in the vicinity of the above, were living a considerable number of vaccinated persons, as may be verified by referring to the tables relating to place of residence.

No. 105. Died not vaccinated 1
Vaccinated 1
No. 107. Vaccinated 2
No. 109. Vaccinated 1
No. 147. Died not vaccinated 1
Vaccinated 1
No. 103. Vaccinated 5
No. 133. Vaccinated 5
Died not vaccinated 2
No. 151. Vaccinated 1
No. 195. Died not vaccinated 1
No. 199. Vaccinated 2
No. 208. Died not vaccinated 1
No. 205. Died not vaccinated 3
No. 198. Vaccinated 10

Résumé.—Vaccinations practiced in Rua Comte d'Eu, 300; died not vaccinated, 8.

3. *Rua José Bernardino.*

No. 1. Died not vaccinated 1
Vaccinations 2

4. *Rua Itapiru.*

No. 61. Died not vaccinated 1
Vaccinations 4
No. 63. Vaccinations 1
No. 49. Died not vaccinated 3
Vaccinations 4
No. 45. Vaccinations 20

Résumé.—Vaccinations practiced, 33; died not vaccinated, 4.

5. *Rua 2 Décembre.*

No. 52. Died not vaccinated 5
Vaccinations 7
No. 50. Vaccinations 4
No. 54. Died not vaccinated 3

In other houses in the same street, 4 vaccinations were made.
Résumé.—Vaccinations, 15; died not vaccinated, 8.

6. *Rua de Vicomte d'Itauna.*

No. 87. Vaccinations 11
Died not vaccinated 1

In Nos. 86, 73, 75, 13, in the vicinity of the above there were eight deaths of unvaccinated persons. In the neighboring houses and throughout the extent of the same street we made one hundred and six vaccinations.
Résumé.—Vaccinations, 106; died not vaccinated, 4.

7. *Rua St. Christophe.*

No. 34. Vaccinations 5
No. 42. Died not vaccinated 1
Nos. 77, 89, 91. Died not vaccinated 3
Nos. 71, 66, 64. Vaccinations 6
Nos. 38 and 44. Vaccinations 11
Nos. 22, 28, 21. Vaccinations 35
No. 18. Died not vaccinated 1

Résumé.—Vaccinations, 58; died not vaccinated, 5.

8. *Rua Laranjeiras.*

No. 37. Died not vaccinated 2
No. 39. Vaccinations 3

9. *Rua Comte de Bomfim.*

No. 7. Vaccinated	20
Died not vaccinated	1
Nos. 3 and 10. Vaccinated	4

Résumé.—Died not vaccinated 1; vaccinated, 50.

10. *Rua des Invalides.*

No. 77. Vaccinations	7
Died not vaccinated	1
No. 94. Died not vaccinated	1
No. 97. Vaccinations	3
Nos. 105 and 107. Vaccinations	11
No. 26. Died not vaccinated	1

Résumé.—Vaccinations, 98; died not vaccinated, 3.

11. *Rua e Largo de Catumby.*

No. 58. Vaccinations	3
Died not vaccinated	1
No. 11. Vaccinations	11
No. 413. Died not vaccinated	1

Résumé.—Vaccinations, 22; died not vaccinated, 2.

12. *Rua Lavradio.*

No. 53. Vaccinations	7
Died not vaccinated	1
No. 51. Vaccinations	10
No. 45. Vaccinated	9
No. 63. Died not vaccinated	1
No. 132. Died not vaccinated	1

Résumé.—Vaccinations, 31; died not vaccinated, 3.

13. *Rua Floresta.*

No. 14. Vaccinated	1
No. 44. Died not vaccinated	1
No. 14. Vaccinations	6
Nos. 26 and 35. Died not vaccinated	2

Résumé.—Vaccinations, 7; died not vaccinated, 3.

14. *Rua Leopoldo.*

No. 6. Vaccinations	13
Died not vaccinated	1
No. 21. Vaccination	1
Died not vaccinated	1
No. 19. Vaccinations	16
No. 17. Vaccinations	10
No. 71. Vaccinations	4
Died not vaccinated	1
Nos. 83 and 85. Vaccinated	2
No. 59. Vaccinated	5
No. 61. Died not vaccinated	2
No. 28. Died not vaccinated	1

Résumé.—Vaccinations, 114; died not vaccinated, 6.

15. *Rua de Areal.*

No. 1. Vaccinated	4
Died not vaccinated	1

Observations.—We could multiply these observations, but we think that they are sufficient to demonstrate clearly the immunity enjoyed by those inoculated. In effect, among nine hundred and fifty-two vaccinations practiced in the epidemic centers, in the same houses from which the dead had been brought out to the number of sixty-six, there was not a single death among those vaccinated.

* * * * * * *

General résumé.—Vaccinations practiced from January to August, 1885, 3,051; died not vaccinated, 278; died vaccinated, 0.

Dr. Freire has omitted to state one very important fact with reference to vaccinations practiced during the period included in this tabular statement. The date of the vaccinations is not given. Fortunately I am able to supply this omission from

his journal containing the names of the vaccinated, which he kindly placed in my hands during my stay in Rio. I find from this record that the inoculations were practiced as follows:

January	392	May	273
February	342	June	813
March	611	July	481
April	139		

Now, it is well known that June and July are months during which yellow fever does not prevail in Rio, and that, in fact, the month of May furnishes as a rule but few cases.

The exposure even in an epidemic year amounts to very little during the months of May, June, and July, and may be considered practically *nil* in a year like 1885, when the whole mortality was only 278 in a city of 400,000 inhabitants. But Dr. Freire has included in his list 1,294 persons who were vaccinated during the healthy winter months of June and July, and who presumably had been exposed during the preceding comparatively unhealthy months of January, February, March, and April. If these 1,294 individuals were protected from an attack of yellow fever by the inoculation practiced in June or July, what protected them from being attacked during the preceding epidemic season? We must insist upon excluding these 1,294 persons from consideration during the year 1885, to which the report under review relates, and we think that it would be quite proper also to exclude those inoculated during the month of May, but will not insist upon this point. We have then to consider the value of the evidence offered by Dr. Freire as regards 1,757 inoculated persons instead of 3,051 included by him in his statistics for the year.

We remarked with reference to those persons selected for vaccination in 1883 and 1884, that "in selecting foreigners, and preferably those who had recently arrived in Brazil, for his first experimental test of the efficacy of his protective inoculations, Dr. Freire has given evidence of his confidence in the method of prophylaxis proposed and of an honest desire to demonstrate its value."

In his inoculations practiced in 1885 we no longer find any evidence of such selection, and, so far as we can judge, the vaccinated persons simply represent the average population of the city of Rio. It is well known that this population includes a large number of persons of foreign birth and especially of Portuguese. The whole foreign-born population probably does not fall below 100,000 persons, but I have not been able to obtain any exact statistics with reference to this point. Dr. Freire vaccinated 2,186 natives and 865 foreigners. Let us assume for the present that the 1,757 persons vaccinated by him during the months of January, February, March, April, and May were comparable so far as susceptibility to yellow fever is concerned with 300,000 of the population of Rio. In this estimate we exclude 100,000 of the population, on the supposition that this number may have enjoyed immunity as a result of having suffered an attack of the disease; 278 deaths in a population of 300,000 gives less than 1 death per 1,000, and there should not have been over 2 deaths among the 1,757 persons inoculated by Dr. Freire during the months of yellow-fever prevalence.

Let us look at the matter in another light. Dr. Freire gives the following table showing the length of residence in Brazil of the foreigners inoculated in 1885:

For a few days	26
For a few months	71
From one year to one year and a half	69
Two years	107
Three years	98
Four years	126
Five years	103
On board ship (de passage)	9
More than five years	256
Total	865

These figures also include the foreigners vaccinated in the healthy months of June and July, and those temporarily in the city (a few days, 26; on board ship, 9), but they will serve our present purpose, which is to call attention to the fact that 759 of the total number given had been in Brazil (and presumably in Rio) more than a year and a half, and had consequently passed through the preceding epidemic year (1884) without contracting yellow fever. If these persons resisted yellow fever during an epidemic in which the number of deaths amounted to 1597, how can it be claimed that they are protected by a vaccination made in 1885, when only 278 deaths occurred, scattered about (sporadic) in a city of 400,000 inhabitants? The same argument applies with greater force to the 359 foreigners inoculated who had resided in Brazil for five years and above (five years, 103; more than five years, 256). Unless the list includes persons who had already suffered an attack of yellow fever, these individuals had passed through the epidemic of 1880 (1,623 deaths) as well as that of 1883 and 1884, without contracting the disease, and we can hardly ascribe their immunity in the comparatively healthy year, 1885, to Dr. Freire's inoculation.

Another important factor in estimating the value of Dr. Freire's statistics is brought out by comparing the ages of those who died of yellow fever during the year 1885 with the ages of those vaccinated. This we have done in the following table, in which the figures as regards the ages of those vaccinated are taken from Dr. Freire's report for 1885, now under review:

Age.	No. vaccinated.	Deaths not vaccinated.
Below ten years	1,697	54
Eleven to twenty years	585	54
Twenty-one to thirty years	384	95
Thirty-one to forty years	238	55
Forty one to fifty years	137	13
Fifty-one to sixty years	41	4
Over sixty years	4	1
Unknown	1	.....
Total	3,051	278

This table shows that 55 per cent. of the vaccinated persons were below ten years of age, while the mortality for those below ten was only 19 per cent. of the total mortality. Or taking the age which gives the largest mortality, we find that only 12 per cent. of the whole number vaccinated were between the age of twenty-one and thirty, while 34 per cent. of the fatal cases were between twenty-one and thirty years of age. It is evident then that the very large proportion of children vaccinated is an element in favor of Dr. Freire's statistics, and not favorable to a fair test of his method of prophylaxis. I find by referring to his records that a considerable number of these children were infants from a few months to two years of age. Even during the prevalence of an epidemic the mortality among such young children is almost *nil*.

Again, if a certain number of deaths had occurred among these young children, it would be a difficult matter to verify the fact. Leaving aside the question of a possible mistake in diagnosis, or an intentional concealment of the cause of death, which is quite common among the class of people inhabiting the cortiços, in which most of Dr. Freire's inoculations have been made, verification is rendered impossible in many cases by the circumstance that the vaccinated persons have remained but a short time in the apartments occupied at the time they were vaccinated, and that the names given in Dr. Freire's lists are in many instances insufficient for their identification. Thus I find in Dr. Freire's record for 1885 and 1886 no less than three hundred and eighteen single names, and of these the name Maria appears fourteen times, Antonio eight times, Joaõ seven times, Josó five times, etc. The ages of the nine entries made under the name Antonio are seven months, eight years, six months, seven years, three months, one year, four years, one and one-half years. In addition to this

there are many double names which are so common as not to serve for identification. The difficulty of obtaining information with reference to the vaccinated persons, and the fact that the addresses given in Dr. Freire's lists can not be depended upon, for identification, when comparison is made with the mortality lists of the city, is illustrated by the results of Mr. Slaughter's investigations heretofore reported, and by my own researches.

In company with Dr. R. Cleary, an American physician, who has been for many years in Brazil, and is now engaged in the practice of his profession in this city, I have visited a large number of the addresses given in that portion of Dr. Freire's report, which has been quoted in full, in which he gives the street and number of the houses in which his vaccinations were made. I did not have time to visit all of the addresses given, but selected those in which a considerable number of vaccinations had been practiced.

Before giving a summary of the results of this investigation it will be well to say something of the *cortiços* or *estalagens* in which most of the vaccinated persons resided. These are the tenements of the poorer classes of the population, and consist of one or two story houses, arranged in parallel blocks, facing each other, on the two sides of a long open court or alley, which is entered from the street by a large door or open gate-way. The cortiços vary very much as to the character of the houses and as to their sanitary condition. Some of them seem to be occupied by industrious, healthy looking laboring people; many by laundresses who occupy the open court in the prosecution of their industry; others by itinerant peddlers, beggars, and all sorts of people from the lowest stratum of the social scale.

I obtain the following information with reference to these cortiços from a report made by the Baron de Ibituruna, inspector-general of hygiene, and published in 1886.

There are in all over eleven hundred cortiços in the city, containing over fifteen thousand separate *quartos* or apartments. The inspector-general of Hygiene gives a very dark picture of the sanitary condition of many of these cortiços. Thus he says of the three hundred and ninety-two located in the parish (*freguezia*) of Sant 'Anna:

"The condition of the cortiços in this vicinity causes amazement, if not horror. There are here tenement courts for which yellow fever has a decided predilection. There are not less than three hundred and ninety-two of these centers of infection. In some men, women, children, mules, and cows live as in the primitive times of Noah's Ark; 4,241 rooms, of which 501 are made of boards, 1,185 in the worst possible condition, and 2,464 in ordinary condition."

Dr. Freire dwells upon the unsanitary condition of these cortiços and upon the fact that his vaccinations have been largely practiced in these centers of infection, as he considers them. It must be admitted that such unsanitary conditions and the aggregation of masses of people in ill-ventilated apartments are favorable to the extension of yellow fever, when other essential factors required for the production of an epidemic are present. But we must call attention to the fact that in 1885 these other factors were absent, as only 278 deaths occurred in a population of 400,000 souls. A very large proportion of these deaths did not occur in the cortiços, and no doubt a considerable number were among sailors from foreign ports, who always furnish a large contingent to the mortality list in non-epidemic years. But suppose the entire mortality had been distributed in the cortiços. There are 1,100 of these, and if the 278 fatal cases had occurred in 278 of these cortiços, one in each, we would have left 822 cortiços in which no fatal case of yellow fever occurred. Let us turn now to Dr. Freire's detailed account of the houses and streets in which vaccinations were made.

1. *Rua de Riachuelo.*

No. 205: Vaccinated	5
Died not vaccinated	1

Upon visiting this cortiço I was informed that no cases of yellow fever had occurred *either among the vaccinated or the unvaccinated* since the vaccinations were

made. My informant insists that only two were vaccinated. I did not inquire as to the total population of this and other cortiços visited, but the report of Baron de Ibitnruna gives the following information with reference to the parish in which this street and the next one in Dr. Freire's list (Comte d'Eu) are situated. In this parish there are 125 cortiços; of these 46 have more than 20 tenements (*quartos*), 26 more than 30, and 18 more than 40. If the average number of tenants for each *quarto* was but three we would have at least sixty persons in each, and in No. 205, at present under consideration, there should be at least fifty-five unvaccinated persons placed under the same conditions as the five vaccinated. These persons did not contract yellow fever, or at least did not die, notwithstanding the fact that a fatal case is reported by Dr. Freire to have occurred at this number.

Dr. Freire's whole argument is based upon the supposition that yellow fever is transmitted by personal contagion, and that the persons vaccinated by him were subjected to a satisfactory test because they lived in the vicinity in which a fatal case of yellow fever had occurred. For me this argument has no weight, as I do not believe that the disease is contracted by contact with the sick. It would be quite as reasonable to vaccinate persons in New York City in tenement houses in which a fatal case of typhoid fever had occurred, or in other houses in the neighborhood, and to claim that they were protected from this disease because they did not contract typhoid fever after being vaccinated.

In our laboratory experiments we are in the habit of preserving one or more animals as a control. If, for example, I inoculate a certain number of animals with the expectation that a certain result will be produced, I place beside them under identical conditions one or more *uninoculated* animals of the same species to serve as a control. If the inoculated animals die and the control animals also die, or *vice versa*, the experiment has no value and must be repeated. Now, in Dr. Freire's inoculations the non-vaccinated persons serve as a control, and fortunately we have a sufficiently large number of these to enable us to form an estimate of the protective value of the inoculations practiced. For example, a death having occurred at No. 205 Rua Riachuelo, Dr. Freire finds among the residents of this cortiço five persons who consent to be vaccinated. There remain in the tenements of the cortiço from fifty to two hundred and fifty* persons unvaccinated. No yellow-fever deaths occur during the remainder of the year either among the vaccinated or the unvaccinated.

I continue now the notes of my personal investigations.

No. 39, cortiço. The proprietor insisted that not more than ten were vaccinated, and says that all except three moved away soon after the vaccinations were practiced. One of the three remaining is said to be an old woman who has lived many years in Brazil, a Portuguese. The other two are Brazilians, born in Rio. None of them have had yellow fever, either before or since vaccination.

No. 43, cortiço. My informant says that the vaccinated were mostly children, and that none of them have had yellow fever, either before or since vaccination.

No. 119, cortiço. All of the vaccinated have moved away. Three are said to have been Italians, and the rest Brazilians. All left soon after vaccination except one Italian. He left in October last. Has not had yellow fever.

Rua de Comte d'Eu.

No. 87. House is vacant.

No. 85. New tenants, who know nothing of former occupants.

No. 93. New tenants, who know nothing of former occupants.

No. 91. House is vacant.

No. 103. New tenants, who know nothing of former occupants.

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* I regret that I did not obtain exact information as to the number of tenants in each cortiço visited by me. This did not occur to me at the time. One of these cortiços, however, which I have since visited (No. 68 Rua do Catete) is said by its proprietor to contain over four hundred tenants.

No. 133. House is vacant.

No. 199. House is vacant.

No. 198, cortiço. Only one man to be found who was here when the vaccinations were made. No further information could be obtained.

In the general résumé Dr. Freire reports that he made three hundred vaccinations in this street, and that there were eight deaths among unvaccinated persons; but in his detailed account, just above, he gives the number of deaths as eleven. Of these seven occurred in houses in which no vaccinations were made and two in houses in which he vaccinated but a single person.

According to the report of the Baron Ibituruna there are twenty-three cortiços in this street, containing from twenty to forty quartos each. It will be seen from this that there must have been a large number of unvaccinated persons in this street who did not die from yellow fever and a considerable number of cortiços in which no deaths occurred. What special value, then, can be attached to the fact stated by Dr. Friere that a non-vaccinated person died during the year at No. 79, and one at 97, and that a considerable number of vaccinated persons lived in the vicinity at Nos. 87, 93, 85, and 91.

Rua de Vicomte d'Itauna.

No. 87, cortiço. Most of those vaccinated have moved away. The proprietor's two children were vaccinated. No cases of yellow fever have occurred in the cortiços since the vaccinations were practiced.

Rua des Invalides.

No. 77. Those who were vaccinated have all moved away.

Nos. 105 and 107, cortiço. Floating population; no information obtained.

Rua de Lavardio.

No. 53. No one in house who was there in 1885.

No. 51. One man, Bernard, aged fifty-eight years; says he was vaccinated; that he had been in Brazil six years; is a Spaniard. *He had yellow fever before he was vaccinated.* He knows that an Italian and his wife and child were vaccinated. They moved away soon after. Did not have yellow fever up to the date of leaving. No other information.

No. 45. House vacated in 1886. Present occupant knows nothing of previous occupants.

Rua de S. Leopoldo.

No. 6, cortiço. Some Italians who were vaccinated have gone back to Italy. There has been but one case of yellow fever since the vaccinations were practiced.

No. 19, cortiço. Proprietor says about twenty were vaccinated. Two who were vaccinated had the fever afterward; both recovered. Those who were vaccinated have all moved away except the proprietor, his wife, and an old man. The proprietor had the fever before vaccination. His wife has lived in Rio fourteen years and has not had fever, either before or since vaccination. The old man has lived in Rio for twenty-eight or thirty years.

No. 17. Three children vaccinated, all born in Brazil. No fever since, either among these or among others in the cortiços.

No. 59, Cortiço. Five children said to have been vaccinated, all Brazilians. No cases among these or others in the cortiço.

We proceed now to analyze the published statistics of Dr. Freire's inoculations made in the year 1885-'86, and in order to do him full justice, I quote extensively from his report:

STATISTICS OF THE VACCINATIONS PRACTICED WITH THE ATTENUATED MICROBE OF YELLOW FEVER FROM SEPTEMBER, 1885, TO SEPTEMBER, 1886.

PART FIRST.

MORTALITY FROM YELLOW FEVER IN RIO DE JANEIRO ACCORDING TO OFFICIAL DOCUMENTS.

The mortality from yellow fever during the epidemic of 1886 was 1,397 persons; foreigners, 1,084; Brazilians, 313.

Nationality of foreigners.—Portugese, 659; Italians, 202; Spaniards, 55; Germans, 30. The others are principally French, English, Swiss, and Hungarians.

Age of the deceased.—From a few months to ten years, 175; from eleven to twenty years, 274; from twenty-one to thirty, 545; from thirty-one to forty, 178; from forty-one to fifty, 109; from fifty-one to sixty, 31; above sixty, 11; age unknown, 51; total, 1,397.

Observations.—Eight per cent. of the deaths were children whose age varied from a few months to ten years. The greater proportion of deaths is included between one and thirty years. This is, then, the period which appears the most favorable for the development of yellow fever. Now, we will see that out of the number vaccinated, which we will give in the second part of our statistics, two thousand six hundred and twenty-four individuals are comprised in this period.

Another fact which must not be lost sight of is that a fourth part of the deaths from yellow fever are among the Brazilians. The same proportion is met with in previous epidemics, as has been shown in the work "Le vaccin de la fiévre jaune, résultats statistiques," published in 1886.

We repeat again that the Brazilians, even those born in Rio de Janeiro, only enjoy a relative immunity, which diminishes according as their place of residence is removed from the city of Rio.

Preventive vaccination is, then, necessary also, in order to confer upon them immunity from the disease. The people of the lower class have happily comprehended this, as is proven by the fact that they form the greater number of those vaccinated in 1886.

We are also convinced that the number of deaths (1,397) from yellow fever is far from the truth, and we may without exaggeration estimate the number of victims at three thousand. Every one knows that for motives of private convenience a great number of physicians disguise in the official bulletins of mortality the well-confirmed diagnosis of yellow fever under the names of bilious remittent fever, pernicious hemorrhagic fever, typhoid fever, abdominal typhus, etc., especially in the "Maisons de Santé," where the sanitary regulations prohibit the treatment of patients attacked with yellow fever. Every day this falsification of diagnosis presents itself, and this abuse, which is not a state secret, continues in view of everybody, notwithstanding the protests of the press. It is to be desired that the sanitary authorities may make all possible efforts for the suppression of this state of things, which constitutes an assured peril. In order to be certain of this fact, one has only to glance at the bulletins of mortality published daily during the epidemic.

The official statement of deaths is as follows: Rio, 887; Jurajuba, 433; Nictheroy, 77.

At Nictheroy (capital of the province, situated on the bay of Rio) the deaths are divided as follows:

Brazilians	44	Spaniards	3
Portuguese	21	Germans	1
Italians	7	Irish	1

Hospital of Jurajuba.—Brazilians, 16; foreigners, 417. At Nictheroy the number of Brazilians exceeds that of the foreigners, because the city is chosen by preference as a place of residence by the Brazilians, who have recently arrived in the province of Rio.

Age of the deceased at Nictheroy.—One year and under, 3; one to ten years, 14; eleven to twenty years, 10; twenty-one to thirty years, 27; thirty-one to forty years, 9; forty-one to fifty years, 9; fifty-one to sixty years, 2; sixty-one to seventy-five years, 3—total, 77.

Out of 313 Brazilians coming from the provinces, there are from Minas, 19; Sao Paulo, 12; Santa Catharina, 2; Rio Grande, 9; Parana, 1; Matto Grosso, 1; Sergipe, 2; Bahia, 1; Pernambueo, 1; Rio de Janeiro, 265.

Included in the preceding figures are eight vaccinated persons who have not obtained immunity—Brazilians, 3; foreigners, 5; as follows:

First, Brazilians.

1. Mariana Candida Pimental; fifty-six years; native of Minas Geras, residing at No. 3, Rue San Francisco Xavier.

2. Carlos, son of Joaquim Pereira Guimaraes; 3 years; residing at No. 16 Rue du Marquez d'Arantes.
3. José, son of José da Costa Vieira; two years, residing at No. 187 bis. Rue Visconde de Sapucahy.

Second, foreigners.

4. Paschoal Rufino, Italian; twenty-one years; residing at No. 8 Rue du Areal.
5. Henri Constance, French; thirty years; residing at No. 29 Rue Evaristo de Veiga.
6. Fernando Argenteiro, Italian; thirty-two years; residing at No. 79 Rue General Caldwell.
7. Antonio Saraiva, Portugese; thirty-three years; residing at No. 7 Rue San Clemente.
8. Maria Emilia Tosta, Portuguese; twenty-eight years; residing at No. 78 Rue de Mattoso.

Then out of 1,572 foreigners vaccinated, 5 deaths; mortality, 0.3 per 100. Out of 4,949 Brazilians vaccinated, 3 deaths; mortality, 0.06 per 100.

We include in these figures all the vaccinated during the two preceding years, who have been carefully observed during the epidemic season.

Second Part.

Preventive vaccinations.—The number of vaccinations practiced with the attenuated culture of the microbe of yellow fever from September 1885, to September 1886, was 3,473, as follows: Brazilians, 2,763; foreigners, 710.

We must insist upon the fact that among the 2,763 Brazilians, there are 489 children of foreigners, all quite young and who in reality may be attached to the 710 foreigners as presenting the same degree of receptivity. Besides, 222 came from different provinces of the interior and from the coast, and who, finding themselves in Rio during the epidemic season, were in the same conditions as foreigners as regards contracting yellow fever, as is shown by the facts observed. The number, then, of vaccinated persons for whom residence can not be invoked as a cause of immunity, should in reality be 1,421.

There remain 2,053 persons of Brazilian nationality whose age varies from some months to sixty years. In this group a great number, by their age, the condition of their dwellings in the quarters most visited by the scourge, are in the most favorable conditions for becoming its victims. Besides, it is evident that immunity is only relative among the adult Brazilians, as is proved by the first part of these statistics, which give in the mortality by yellow fever 253 Brazilians in the city of Rio, 16 in the hospital of Jurajuba, and 44 in the city of Nictheroy. This makes the number of deaths 313.

The vaccinations have been made especially at the points where the disease has developed itself with the greatest intensity. The greater part of those vaccinated resided in the cortiços or estalagens (a kind of low one-story houses resting upon the soil) in which the hygienic conditions are deplorable. All the physicians agree in declaring that these houses constitute the best *foyer* for the production and especially for the propagation of yellow fever.

Nationality of the vaccinated.—Brazilians, 2,763; Portuguese, 492; Italians, 115; French, 13; Spaniards, 43; Paraguayans, 16; Russians, 1; Swiss, 3; Germans, 5; Montevideo, 3; Argentine Republic, 4; Chilian, 1; United States, 2; Belgian, 1; African, 11.

Descent of 489 individuals born of foreign parents, included in the Brazilian section.—Children of Portuguese, 435; of Italians, 24; of Spaniards, 17; of Germans, 8; of French, 3; of Paraguayans, 2.

Indication of the Provinces from which 222 individuals came who are included in the Brazilian section.—Province of Rio de Janeiro, 83; Sao-Paulo, 31; Bahia, 29; Minas-Geraes, 16; Pernambuco, 14; Rio Grande do Sud, 11; Maragnan, 7; Sergipe, 5; Santa-Catharina, 5; Ceara, 5; Espirito-Santo, 3; Piauhy, 2; Matto-Grosso, 2; Alagoas, 1; Para, 1; divers other provinces, 4.

It is notorious that the fact of residing some leagues from the city of Rio de Janeiro constitutes for all these individuals a much greater susceptibility to yellow fever. A great number of cases have been thus verified during the last epidemic. We have had also to regret the death of Dr. Telles, residing at Jacarepagua, who contracted yellow fever during a very short stay which he made in Rio. Among the vaccinated Brazilians we include eighty individuals coming from the Province of Rio de Janeiro, that is to say, dwelling some leagues from the capital.

Age of the vaccinated persons.—From a few months to ten years, 1,491; from eleven years to twenty years, 606; from twenty-one to thirty years, 527; from thirty-one to forty years, 391; from forty-one to fifty years, 296; from fifty-one to sixty years, 133; above sixty years, 29.

This shows that there is no danger in practicing the inoculations upon children, even very young. Besides, we call attention to the fact, already referred to, that the greater proportion of the vaccinated are aged from a few months to thirty years; that is to say, at the age when the mortality from yellow fever attains its largest figure. (See the table of mortality in the first part.)

Time of residence of the foreigners in Rio (including in this class the individuals born in the Province).—A few days, 53; a few months, 124; from one year to one and one-half years, 77; two years, 82; three years, 93; four years, 61; five and six years, 115; more than six years, 327.

Many of these 327 had only seven to eight years of residence, including the young persons engaged in commerce and those pursuing their studies.

REMARKS.

Among the foreigners vaccinated are the crews of several foreign vessels, the captains of which came themselves to claim the benefit of inoculation. We will mention particularly Captain Vallé of the sailing-ship *La Breteche*, from the port of St. Nazaire, whose conduct was beyond all praise.

Let us add yet an important observation made at the marine hospital of Jurajuba, which is especially provided for the reception of yellow-fever patients. Three who had been previously vaccinated were sent by the sanitary authorities to this hospital, but the disease was very benign, and the three persons recovered in a few days, while four hundred and thirty-three *non-vaccinated* became the victims of the *microbe amaril* in the same hospital.

General résumé.

Vaccinations practiced in 1886	3,473
Died vaccinated	7
Vaccinations practiced in 1885	3,051
Died vaccinated	1
Total vaccinated	6,528
Total deaths vaccinated	8

Mortality among the vaccinated 0.1 per 100.

Mortality of the non-vaccinated, from the official figures, due to yellow fever, 1,389 in 1886; 278 in 1885; total, 1667.

Thus, as may be judged from what precedes, the immunity conferred by the attenuated microbe, without being absolute, has nevertheless produced very satisfactoy results.

Taking into consideration the epidemic centers, in the midst of which the vaccinated resided, we may estimate the number of individuals exposed to contract yellow fever at the maximum figure of 160,000. On comparing this figure with that of the vaccinated and the number of deaths among the vaccinated with the number of deaths among the non-vaccinated we calculate that the mortality is 1 per 1,000 for the vaccinated, and 1 per 100 for the non-vaccinated.

We have quoted extensively from this last report of Dr. Freire in order to do him full justice by allowing him to state his own case. We shall now proceed to show that his statistics are fallacious, and that the percentage of mortality among the vaccinated, which he finds to be ten times less than among the non-vaccinated, results from a misuse of the statistical method and from a number of factors, which are favorable to Dr. Freire's statistics as he has stated them, but not to a fair test of his method of prophylaxis.

In the first place, we would call attention to the fact that while during the comparatively healthy year, 1885, the immunity among the vaccinated of that year is said to be complete (see report of 1885), the number of deaths during the epidemic year which followed is stated by Dr. Freire himself to have been eight. Taking all of the vaccinated of the two years, and without making any allowance for the considerable number of persons vaccinated who had, no doubt, left the city before the epidemic of 1886 occurred, Dr. Freire with a total of 6,524 vaccinated, and a total of 8 deaths, makes the proportion 1 per 1,000. This is equivalent at the outset to an addition of 1,476 persons to the number vaccinated, who being imaginary persons and not having been exposed to the epidemic influence simply aid in rounding up the general percentage of mortality in Dr. Freire's favor to the even figure of 1 per 1,000. This is but one of many factors which go to make up this favorable showing. Refer-

ence to Dr. Freire's manuscript journals, which he kindly placed in my hands, shows that of the total number vaccinated during the two years, 4,465 were vaccinated prior to the epidemic of 1866, that is to say, before the 1st of January, 1886. How many of these left the city before the outbreak of the epidemic, how many were only temporarily in the city when vaccinated, how many died from other diseases, I can not say; but it is a significant fact that of the 3,051 vaccinated prior to August, 1885, Dr. Freire has only 1 fatal case to report, while out of 460 persons vaccinated in January and February, 1886, he reports 5 deaths, a mortality of more than 1 per cent., which he gives as the general mortality among the non-vaccinated. This is not apparent from Dr. Freire's own statement of the case, but is nevertheless true, as I shall proceed to show. In his report, which we have just given in full, he does not give the date of the vaccination of these individuals, but upon referring to his manuscript journal for 1886, I find that No. 3 of his list, José, son of José da Costa Vieira, was vaccinated February 12, 1886; No. 4, Paschoal Ruffino, on the 6th of February, 1886; No. 5, Henri Constance, on the 1st of January, 1886; No. 6, Fernando Argenteiro, on the 20th of February, 1886; and No. 7, Antonio Saraiva, on the 12th of February, 1886. The same manuscript record for 1886 shows that during these two months—January and February, 1886—the total number vaccinated by Dr. Freire was 460. That is to say, the mortality among those vaccinated during these two months was more than 1 per cent. On referring to the mortality lists of the city for the same two months, I find the total number of deaths to have been 369, which in a total susceptible population of 160,000 (Dr. Freire's estimate), would give a mortality of one in 436.

In a communication made to the French Academy of Sciences on the 4th of April, 1887, and published in the "Comptes rendus" of that date, Dr. Freire says: "In this number of 1,675 deaths there are included 8 vaccinated persons and 1,667 not vaccinated. Before going any further we ought to remark that the vaccinated who died during the epidemic were inoculated at the moment when the method of inoculation was yet imperfect." Upon reading this sentence the natural inference is that these individuals had been inoculated by Dr. Freire at the outset of his attempts in this direction. To my surprise, I found upon referring to his record that five out of the eight had been vaccinated in January and February, 1887, and that consequently the sentence quoted, which has all the authority of a well-considered communication made to the French Academy of Sciences, involves the admission that the 4,465 persons vaccinated prior to this time had been vaccinated by an imperfect method.

Again I find that in 1886 as in 1885 Dr. Freire has included in his statistics a large number of persons who were vaccinated after the termination of the epidemic, and whose exposure was but little greater than that of the 1,476 imaginary persons who must be added to his list in order to give the mortality of 1 per 1,000.

Dr. Freire has not given us the date of his vaccinations in his elaborate presentation of his statistical results, but I find from his manuscript record that they were distributed throughout the year as follows—I place in a paralled column the figures showing the total mortality from yellow fever during the period:

Month.	Vaccinations.	Total deaths from yellow fever.
1886.		
January	84	135
February	376	234
March	253	347
April	167	220
May	945	48
June	21	18
July	57	9
August	3	2

This table shows that during the epidemic period from January 1 to April 30 there were 880 vaccinations, and during the same period 936 deaths occurred from yellow

fever, while during the months of May, June, July, and August, when the total mortality was but 77, the number of vaccinations was 1,026; *i. e.*, a majority of the vaccinations was practiced after the epidemic season was over, and upon persons who, no doubt, had for the most part passed through the epidemic season without contracting the disease.

We turn now to the age of the vaccinated persons. Dr. Freire says, in his report first quoted: "The greater proportion of the deaths is comprised between one and thirty years. This is, then, the period most favorable for the developement of yellow fever. Now, it will be seen that among the number vaccinated, which we give in the second part of our statistics, 2,624 individuals are comprised in this period." But Dr. Freire has elsewhere shown us that the age which gives the greatest mortality is from twenty-one to thirty years. Let us then see what proportion of the vaccinated are included in these limits. Reference to his tables shows the deaths between twenty-one and thirty years of age to have constituted 39 per cent. of the entire mortality, while only 15 per cent. of the vacinated fell within these limits of age. On the other hand 43 per cent. of the vaccinated were less than ten years of age, while the mortality for this period was only 12.5 per cent. of the entire mortality. We note also that a large number of the children vaccinated were infants below two years of age.

Let us turn now to the table given by Dr. Freire on page 11 of the report under consideration:

Time of residence of the foreigners in Rio (including in this class the individuals born in the provinces.)—A few days, 53; a few months, 124; one year to a year and a half, 77; two years, 82; three years, 93; four years, 61; five and six years, 115; more than six years, 327.

We remark, first, that it is not apparent from Dr. Freire's figures how many of these foreigners were vaccinated after the termination of the epidemic, or how many of the fifty-three who had been in the city but a few days were travelers who did not remain many days after their vaccination, and who kept away from infected localities while in the city. No doubt the crews of certain foreign vessels, to which Dr. Freire refers on page 15, are included in this number. We have no data as to the period of the year when these vaccinations were practiced, or as to the exposure of the vaccinated persons after they were vaccinated.

As an illustration of the insufficient nature of the evidence in the case of persons temporarily in the city, I will cite the case of an American physician, engaged in missionary work at San Paõlo. This gentleman published an account of his case in one of our medical journals which gave me the impression that after being vaccinated by Dr. Freire he had passed through an epidemic of yellow fever in Rio. I learn, however, from the best authority, that he only remained in Rio a few days after he was vaccinated, and that instead of being exposed in the infected parts of the city, he spent his nights, at least, at Petropolis, which is the harbor of safety for foreigners, up to the date of his sailing for the United States. Moreover, this gentleman had formerly resided in the city of Rio for several years. His escape from an attack under these circumstances can scarcely be attributed to the vaccination practiced by Dr. Freire. As a matter of fact numerous unvaccinated foreigners passed through the entire epidemic season of 1886 without contracting yellow fever. This is true, for example, of our consul-general at Rio, and of the vice-consul, who both came from the United States in 1885; who went to their office in the heart of the city every day throughout the epidemic season, and who did not spend their nights at Petropolis, but remained within the city limits.

My inquiries have developed the fact, also, that a large number of Americans, Englishmen, and Germans engaged in business in Rio have had a similar experience. Many of these gentlemen have passed through several successive epidemics without suffering an attack. This is shown by the table which we have quoted above from Dr. Freire's report. Out of a total number of nine hundred and thirty-two foreigners and natives born in the provinces vaccinated in 1886, six hundred and

seventy-eight, or 71.6 per cent., had resided in the city more than two years, and four hundred and forty-two, or 47.4 per cent., for five years and above. That is to say, over 70 per cent. of the whole number had already passed through one or more epidemics of yellow fever without contracting the disease prior to the time when they were vaccinated by Dr. Freire, unless he vaccinated persons who had previously suffered an attack, in which case the experiment would evidently be without value. Among the vaccinated foreigners are a large number who had resided in Rio for ten years and above, and some even as long as twenty-five years.

By referring to the mortality lists of the Jurajuba hospital for 1886 and 1887, I find that out of 194 cases in which the time of residence in Brazil is given 117 had been in the country for one year and below, 36 from one to two years, and 41 for three years and above. In other words, more than 78 per cent. of the fatal cases were among foreigners who had been less than three years in the county, while only 36 per cent. of the foreigers vaccinated by Dr. Freire had been less than three years in the country.

The total number vaccinated in 1886 is given by Dr. Freire as 3,473, of whom 2,763 were native Brazilians and 710 foreigners. That is, the foreigners constituted about one-fifth of the total number vaccinated. But the total number vaccinated during the epidemic season from December 1, 1885, to April 30, 1886, was only 922. If the foreigners have the same ratio to this fractional part of the vaccinated as to the whole number we would have as vaccinated during the epidemic season 185 foreigners, over two-thirds of which number had resided in the city at the time of the previous epidemic (1884).

Let us now turn to Dr. Freire's tabular statement of the streets and houses in which vaccinations were practiced. This appears at first glance to be a strong statement of his case, but this appearance is illusory and depends upon the omission of an important element, viz, an account of the number of unvaccinated persons who were placed in the same conditions as the vaccinated and who did not contract yellow fever. I have called attention to this point in my review of Dr. Freire's statistics for the year 1885, and it is unnecessary to repeat in detail the statements made there. Let us make, however, an analysis of a different kind. We find by reference to page 12 of his published report for the year 1886 that the whole number vaccinated in the streets mentioned on this page was 810=23.3 per cent. of the whole number vaccinated. The number of deaths in the same streets was 110=7.8 per cent. of the total mortality. On the other hand, we find by reference to page 13 that the mortality in "different streets in the center of the city" was 134=9.6 per cent. of the entire mortality, while the number vaccinated in this part of the city was only 65= 1.8 per cent. of the total number vaccinnated. Again we find that nearly 12 per cent. of the vaccinated resided in Nictheroy, a city which has a population of over 20,000, not counted in the general estimate of 400,000, which is accepted as the population of the city of Rio in the statistics of the central board of health. The number of deaths in Nictheroy was, however, less than 6 per cent. of the total number of deaths.

Finally, as to the nationality of the vaccinated. 2,763 are said to be Brazilians and 710 foreigners. Dr. Freire insists on including with the foreigners 222 Brazilians who came from the provinces, and states in detail the various provinces from which they came. The inference is therefore justified that, with this exception, the Brazilians vaccinated are natives of the city of Rio. That is to say, 2,541 of the vaccinated persons were born in the city of Rio. This number includes natives of all colors and all shades of color. The proportion of natives born in the city is, then, about 72 per cent., and that of foreigners and natives born outside of the city about 28 per cent. Now, this is probably a larger proportion of natives born in the city than would be found in a correct estimate of the entire population. The population of foreign birth is estimated at 100,000. The number of deaths from yellow fever among the foreign population in 1886 is given by Dr. Freire as 1,084, which gives a proportion of 1 to 92.2.

Dr. Freire, including all of the foreigners vaccinated in 1885 and 1886, without allowing for those vaccinated after the termination of the epidemic, or those who had left the city before it commenced, or those who ran away during its prevalence, admits a mortality of 5 out of 1,572 foreigners vaccinated, which gives a ratio of 1 to 314. In the same way, admitting three deaths among the total number of 4,949 Brazilians vaccinated in the two years, he finds the mortality to be 0.06 per 100 = 1 to 1,666. The entire mortality among the native population in 1886 was 313, which in a population of 300,000 gives a ratio of 1 to 958. When we consider the several points heretofore referred to, it will be seen that these figures can not be accepted as establishing Dr. Freire's claim to have discovered a method of preventing yellow fever by inoculations with his "attenuated microbe," even when we take his own statement of the number of deaths. But, as I shall show later, there is good reason to believe that Dr. Freire's list of eight vaccinated persons who succumbed during the epidemic of 1886 is by no means complete.

In the first place, with the best possible will to discover all of the fatal cases, it would be hardly possible to do so. My own investigations, heretofore detailed, show that the population of the cortiços, in which Dr. Freire's vaccinations have for the most part been made, is a floating population, and that after the lapse of a little time it is often impossible to obtain any information with reference to the vaccinated persons. The identification by residence can, therefore, not be depended upon when a name in the official mortality lists corresponds with that of a vaccinated person.

For example, Dr. Freire vaccinated July 6, 1885, a woman named Ludovina de Jesus, a Portuguese, aged forty-three years, living at 45 Rua S. Luzia. On the 15th or February, 1886, according to the official mortality lists on file at the office of the central board of health, a woman of the same name and nationality, aged forty-six years, died at Rua de Senador Verguiro, No. 12.

In company with Dr. Cleary I visited both of these addresses. The occupant of the house where Ludovina de Jesus died says that she was a washerwoman who had only been in his house a few days at the time of her death. He knows nothing of her former history. At No. 45 Rua S. Luzia, where, according to Dr. Freire's manuscript journal, a Ludovina de Jesus was vaccinated, I could obtain no information. The number given is that of a cortiço containing numerous apartments. The proprietor says there is no one in his rooms who occupied them in 1885, and he knows nothing of the person named.

Again Dr. Freire's books show that *Maria dos Anjos*, aged seven years, Portuguese, was vaccinated March 24, 1885, at Rua de V. d'Itauna, No. 165.

The mortality lists show that a child of the same age and nationality, named *Maria dos Anjos e Silva*, died January 28, 1886, at No. 372 Rua d'Alfendega. This address was visited and I was informed by the present occupant that the father of the child had returned to Portugal. No further information could be obtained. Upon visiting the house where the vaccination was practiced I could obtain no information. The place is a cortiço; the proprietor and his tenants are all new people and know nothing of the former occupants of the place.

Again, *José de Oliveira Coelho*, a Portuguese, aged forty-two years, appears in the official record as having died at Rua de Carvalho de Sá, No. 4, on the 15th February, 1886.

Dr. Freire's books show that *José de Olivera*, a Portuguese, aged forty-two years, was vaccinated June 5, 1885, at No. 10 Rua da Alfendega. Upon visiting the latter address the house was found to be empty and undergoing repairs. The proprietor of the cortiço where the death is reported to have occurred denies that a person of this named died in his apartments in 1886. No further information could be obtained. I did not find time while in Rio to make any further efforts to identify individuals by visiting the address given in the mortality lists, and in those kept by Dr. Freire, in cases where the name, age, and nationality corresponded nearly enough to suggest identity. But in a partial comparison of these lists I found three cases in which the probability of identity seems to be very great. In each case the individuals were

vaccinated in 1885 and in each case the age given in the mortality lists of the following year is, as it should be, one year more than that of the individual vaccinated. The names are as follows:

1. *Antonio Borges;* ten years of age; Portuguese; vaccinated in 1885 (No. 1882); residence, Rua S. Christovão No. 66. *Antonio Borges Godinho;* eleven years of age; died March 14, 1886; residence, Rua S. Christovão No. 77.

2. *Antonio Gomes da Silva;* sixteen years of age; Portuguese; vaccinated in 1885 (No. 31*); residence, Rua Senador Euzebio No. 64; one year in Brazil. *Antonio Gomes da Silva;* seventeen years of age; Portuguese; died May 21, 1886; residence, Rua do Barão de Itapigipe No. 30.

3. *Roza Maria Bastos;* nine years of age; Portuguese; vaccinated in 1885 (No. 1898); residence, Rua Miguel de Frias No. 30. *Roza;* ten years of age; Brazilian; residence, Rua Miguel de Frias No. 30; died February 12, 1886.

I can scarcely doubt that these three cases and that of Ludovina de Jesus should be added to the list given by Dr. Freire of persons vaccinated in 1885 who died in 1886. The cases of *Maria dos Anjos* and *José de Oliveira* may be considered cases of probable identity. To these I may add the following:

1. *Manuel Alves Pinto;* twenty-seven years of age; vaccinated in 1885 (No. 347); residence, rua da Sant' Anna, No. 76. *Manuel Alves;* twenty-eight years of age; Portuguese; died in the Jurajuba hospital in 1886.

2. *José da Costa;* twenty-six years of age; Portuguese; vaccinated in 1885 (No. 3); residence, rua Miguel de Frias, No. 40. *José Ignacio da Costa;* aged twenty-six years; Portuguese; died April 15, 1886; residence, rua Estacio de Sá, No. 40

3. *Leonor;* four years of age; Brazilian; vaccinated in 1885 (No. 736); residence, rua Conde d' Eu, No. 137. *Leonor;* five years of age; Brazilian; died March 2, 1886; residence, rua do Evaristo da Veiga, No. 65.

4. *Maria Augusta;* sixteen years of age; Portuguese; vaccinated in 1885 (No. 2729); residence, Senador Pompeo, No. 4 A. *Maria Augusta Pacheco;* aged sixteen years; Portuguese; died March 15, 1886; residence, rua dos Invalidos, No. 99.

5. *Emelia;* four years of age; Brazilian; vaccinated in 1885 (No. 1507); residence, rua General Caldwell, No. 105. *Emelia;* five years of age; Brazilian; died March 5, 1886; residence, rua de S. José, No. 68.

6. *Elvira;* three years of age; Brazilian; vaccinated in 1885 (No. 81); residence, rua General Caldwell, No. 114. *Elvira;* four years of age; Brazilian; died February 20, 1886; residence, rua do Lavradio, No. 170.

Another *Elvira;* aged three years; Brazilian; died March 4, 1886; residence, rua do Senador Pompeo, No. 149.

A complete research would no doubt add considerably to this list, and a visit to the addresses given above might in some cases show that the correspondence in name and age was simply a coincidence, and that the vaccinated person is still living. In other cases, judging from my efforts in this direction already reported, it is probable that no information would be obtained and the question of identity would still remain in doubt. Since my return from Brazil I have received a letter, dated January 14, 1888, from Dr. Cleary, an American physician practicing in Rio, in which he says:

"I have discovered another case for you. A French-American named Bitté, employed by Robin in the rua d' Assemblea, and living at the Hotel Commercine, was inoculated by Dr. Freire in 1885, and some weeks after died of yellow fever. This I tell you on the authority of the book-keeper, and I am quite sure of its truth."

In Dr. Freire's report under review, he says, on page 7: "We include in these figures all the vaccinated during the two previous years *who have been carefully observed during the epidemic season.*"

That portion of the sentence which I have italicised surprises me exceedingly. From what has been said it will be seen that a careful observation of the floating

* The number is that given in the list published in the Jornal de Noticias.

population of the cortiços in which most of the vaccinated persons resided would be practically impossible, even with a large force of inspectors at command.

Dr. Freire himself did not find time to make the vaccinations among these poor people of the cortiços, but delegated this work to certain apothecaries. One of these, Mr. Telles, informed me that he had himself vaccinated between three and four thousand persons. He also communicated the startling information that none of those inoculated with the "attenuated microbe" of yellow fever had contracted small-pox during the recent epidemic in Rio, leaving me to infer that the vaccine was a protection against both diseases. This intelligent (?) apothecary, a mullato, recorded a large portion of the statistics which Dr. Freire has tabulated, and we are certainly at liberty to question whether his record is complete and accurate in all particulars. For example, it would be quite natural, and perhaps excusable to write *Maria dos Anjos* instead of *Maria dos Anjos e Silva*. As a matter of fact, a large number of the vaccinated persons are designated by a single name, *e. g.*, Antonio, José, Maria; or by two baptismal names which do not include the family name, as, *e. g.*, Maria José, etc. Under these circumstances, and in view of the fact that many of the vaccinated did not remain in the city, we can not allow Dr. Freire's assertion that all the vaccinated "have been carefully observed during the epidemic season" to pass unchallenged.

Our analysis leads us to the conclusion that *there is no satisfactory evidence that Dr. Freire's inoculations have had any prophylactic value.*

THE YELLOW FEVER "GERM" OF DR. CARMONA Y VALLE, OF MEXICO.

Dr. Manuel Carmona y Valle has given an account of his researches and supposed discovery in his memoir, entitled: "Leçons sur l'étiologie et la prophylaxie de la fièvre jaune," Mexico, 1885.

I am indebted to Dr. Carmona for a copy of this work, which he presented to me at the time of my visit to Mexico. The following inscription, signed by him, is upon the title-page and is a frank acknowledgment that the author has modified his views very considerably with reference to his earlier observations:

A M. le Dr. Sternberg:

Quoiqu'il soit nécessaire de modifier toute la partie relative à la morphologie et aux cultures du micro-organisme.

Dr. Carmona y Valle.

Mexico, *le 26 septembre* 1887.

In view of this acknowledgement I do not consider it necessary to review at length the work of Dr. Carmona, but will quote the résumé which he has given in his "Septième Leçon" in order to show the morphology of his *Penerospora lutea* as he conceived it at the time this work was written.

Admitting but two phases in the development of the fungus which produces yellow fever, I shall recapitulate the succession of the phenomena which occur, in order to fix them well in your memory.

Let us take as point of departure the urine eliminated by yellow-fever patients. It contains, as you know, a great number of zoospores, or very small granulations, endowed with motion—*douées d'un mouvement propre*—and which only measure a thousandth of a millimeter in diameter. These granules are united in pairs, and little by little they unite into a single one, which grows gradually. This becomes opaque, and assumes a gamboge-yellow color by reflected light, and yellowish-red as seen by refraction.

Some of these spores, the dimensions of which are very variable, attain sometimes twenty-four thousandths of a millimeter in diameter. They hibernate in many cases for a longer or shorter time, and on other occasions they germinate at once and

produce the *mucédine* which we have described. The spores of this *mucédine* in penetrating into the animal economy give birth to a *peronospore*, in the organic dilatations of which appear a great number of zoosporangia filled with zoospores. When the little zoosporangial pouches are ruptured, the zoospores are distributed throughout the economy, and are nourished at the expense of the elements which they encounter in the cells of all the organs. In the kidneys they destroy the epithelium of the tubules, and by reason of their number obstruct the interior of the uriniferous canals, and determine thus a diminution of the quantity of urine and difficulty in the elimination of the urea. From the accumulation of this principle in the blood comes the acute uremia, accompanied by all its symptoms. In addition, the nerve cells, the muscular fibers of the heart, the blood globules, and the hepatic cells, injured in their turn by the great number of parasites which are nourished at their expense, determine the pathological complexus known under the name of yellow fever. When later, after their union, the zoospores form the yellow spores, these give to the patient or to the corpse the typical color which we know. These same zoospores which exist in the urine, in the vomited matters, and in the feces form the seed which later will reproduce the *mucédine*, and with it the same circle which we have already described. It is unnecessary to tell you that the corpse is a veritable nursery of zoospores, and for that reason a focus of germs capable of reproducing the disease.

The discovery of the *mucédine*, which at first presented some difficulties because of the manner in which I regard the germ of yellow fever, came later to explain to me certain phenomena which had seemed to me up to that time to be difficult of comprehension.

I wish to speak of the mode of transmission of yellow fever. You know that it can not be considered as contagious in the full acceptation of the word, or, in other terms, that it does not appear to be transmitted from individual to individual, as occurs in typhus and other maladies which are directly transmissible, or contagious. We see yellow fever attack indifferently persons who are in direct contact with the sick, or others who, holding themselves removed, live in the same locality. Besides, a patient attacked with yellow fever never transmits the disease to persons who do not live in conditions suitable for the development of the germ. Persons attacked with yellow fever often come from Vera Cruz to Mexico, and we have never seen them communicate the disease to those who surround them, as could not fail to happen if the disease could be transmitted directly from individual to individual.

The discovery of the *mucédine*, a variety intermediary between the primitive spore and the *peronospore* which produces the malady, furnishes a means of explaining this mystery. The zoospore, or the spore given off by the patient, can not directly give yellow fever, because it does not immediately produce the *peronospora lutea;* and it is for this reason that the sick person can not communicate immediately the disease with which he is attacked. This is why the appearance of yellow fever is impossible in the localities where the tellurico-atmospheric conditions do not permit the development of the *mucédinée*.

At the time of my visit to Mexico Dr. Carmona had abandoned the idea of a genetic relation between the so-called zoospores, found by him in the urine of yellow-fever patients and the hyphomycetous fungi above referred to under the name of *peronosporée* and *mucédinée*. He, however, adhered to the belief that the "zoospores" were directly concerned in the etiology of yellow fever, and believed that he had demonstrated by recent observations that these "zoospores" develop into a bacillus.

According to Dr. Carmona's present idea the zoospores develop into bacilli, and these again break up into zoospores. This he believed to have proved by culture-experiments in which he obtained from the urine first a culture containing the zoospores, while later, on making a second culture from this stock, he found upon microscopic examination only bacilli. He was kind enough to show me a stained preparation of the zoospores and of the bacilli. I recognized at once in the former a micrococcus which does not differ in its morphology from one found constantly in urine which has undergone alkaline fermentation—the *M. ureæ* of Cohn. Evidently Dr. Carmona's inference that this micrococcus and the bacillus which developed in his cultures from the same source represent different stages in the life-history of a single organism is a mistake. I have proved this by isolating the two organisms from a culture which he gave me at the time of my visit to his laboratory. Moreover, this culture contained numerous other organisms, including one or more species of hyphomycetous fungi.

Bacterio'ogists know very well that it often happens when a culture-medium is in-

oculated with impure stock that one organism—and very commonly a micrococcus—takes the precedence, and that upon microscopical examination, this, by reason of its abundance, may appear to be the only organism present, but that later other organisms present may develop in their turn, while the first disappears or is found in comparatively small numbers. It is in this way that we explain the alternation of micrococci and bacilli obtained by Dr. Carmona in his cultures. A few spores of the bacillus present in the first instance might easily escape notice.

All bacteriologists will agree that the finding of micro-organisms in the urine, when they have not been demonstrated to be present in the blood and tissues, can have but little significance in the absence of an exact demonstration of their specific pathogenic power. We now know that a variety of micro-organisms are constantly present upon the surface of the mucous membrane at the extremity of the urethra, and that however carefully the sound and the receiving vessel may be sterilized, it is practically impossible to obtain urine from the bladder free from these micro-organisms without first sterilizing the urethral canal. The writer recently passed a little urine into a sterilized test-tube, the cotton stopper of which was removed for an instant and immediately replaced. The test-tube was placed in a culture-oven for 48 hours, at a temperature of 98° F., and at the end of this time a drop of the contained urine, which gave the usual evidence of having "broken down," was used to inoculate a series of Esmarch tubes. From these no less than seven distinct micro-organisms were obtained.

A more complete analysis of the micro-organisms commonly found in the urethra and in urine from healthy individuals is that made by Lustgarten & Mannaberg*

The authors examined the extremity of the normal human urethra. After cleaning the glans with a piece of cotton wet with a solution of carbolic acid, they introduced a little spoon of platinum, sterilized by heat, into the *fossa navicularis*, and the traces of mucus secretion adhering to this were conveyed to a culture-medium and the micro-organisms present isolated by Koch's plate method. Ten different micro-organisms were recognized by microscopic examination which were found in greater or less abundance in eight cases carefully studied. They found almost constantly bacilli which in all respects resemble the "smegma-bacillus," but which they did not succeed in cultivating. In the second place they describe a diplococcus which was met with in perfectly healthy individuals and which in form and dimensions exactly resembles the "gonococcus" of Neisser. The *Staphylococcus pyogenus aureus* and *Diplococcus subflavus* of Bumm & Flügge were present, together with a number of species not previously described. One named *Streptococcus giganteus urethræ* consisted of long chains of round elements, which just before division showed a transverse line, and after division presented the appearance of oval diplococci. The bacteriological examination of the urine showed that whenever this was permitted to pass through the urethra it contained a variety of micro-organisms, which, however, were for the most part not able to develop in normal urine, which is an acid fluid, and therefore not suited to serve as a culture-medium for very many species of bacteria. The observations of the authors named convinced them, however, that normal urine as it exists in the bladder is free from micro-organisms.

It is evident, from what has been said, that we have no guaranty that micro-organisms found in the urine of yellow-fever patients or in cultures made from such urine are from the interior of the bladder, unless the urine has been collected by a method which excludes the possibility of contamination by these various micro-organisms lying upon the surface of the mucous-membrane at the extremity of the urethral canal. I do not find any satisfactory evidence that the required precautions were taken by Dr. Carmona, or by those who collected urine for him in Vera Cruz and elsewhere.

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* Ueber die Mikroorganismen der normalen männlichen Urethra und des normalen Harnes. *Vierteljahrsschrift für Dermatologie und Syphilis*, 1887, No. 4.

The writer fully appreciated this difficulty, when in Havana, in 1879, and therefore did not attach any special significance to the presence of various micro-organisms observed in yellow-fever urine collected in sterilized vessels. Such urine examined immediately after collection was not found to contain any bacteria, but after it had been standing in the laboratory for a short time there was an abundant development of various forms. My photographs show a bacillus in pairs, with rounded ends; a bacillus with square ends in long chains; budding torula-cells; spherical organisms, etc. Now as albuminous urine is a suitable culture-medium for a variety of micro-organisms, and as the urine examined by myself in Havana and by Dr. Carmona in Mexico came from infected localities, it is quite possible that one or the other of the micro-organisms which we have encountered in this fluid is the genuine yellow-fever germ; but, if so, there is no evidence or record which goes to prove that such is the case.*

DR. CARMONA'S ZOOSPORES.

Dr. Carmona has given a remarkable account of the resisting power of his zoospores to heat and chemical agents. He says on page 199 *et seq.:*

I have already said to you that notwithstanding the resemblance of these microbes with certain bacteria of putrefaction, they differ from these by their aérobic property. * * * But they can likewise live outside of the influence of the air, and in order to prove it to you it will suffice to recall to you that I have encountered millions, gifted with their peculiar movements, in a preparation of the liver preserved for three years in Canada balsam perfectly dry. Consider that these organisms, inclosed between two plates of glass, and in Canada balsam, were perfectly protected from contact with the air, as is every preparation preserved in balsam. Then, if after remaining three years in this condition they preserve their proper motion, it is clear that their organization may be preserved without the presence of oxygen.

You can form a general idea of the resistance of our zoospores in recalling the different liquids which acted upon the preparation before it was completely finished. The liver was macerated for a month in Müller's fluid, and as at the end of this time it was not found sufficiently hardened, it was put for eight days in a solution of chromic acid. Then thin sections were made with a microtome which were passed through the picrocarminate of ammonia to stain them. After that the sections were put into absolute alcohol to dehydrate them, then into turpentine to make them transparent, and finally they were fixed in Canada balsam dissolved in chloroform.

On another page (60), Dr. Carmona explains that in the experiment above referred to he first removed the cover-glass from the preparation, then detached the section of liver and macerated it for some minutes in distilled water, after which he says:

I placed it then upon a slide and examined it under the microscope to see the yellowish conglomerates inclosed in the hepatic capillaries. I saw the granular matter entirely compact and did not remark any movement in the granules. I then took a simple microscope and endeavored to disaggregate the granular conglomerate by means of a needle, then adding a drop of water I again examined it with a suitable power (400 diameters). I noted then that the detached granules resumed their oscillatory movements as if they had never been inclosed in the Canada balsam. These experiments were made in presence of Dr. Miguel Alvarado and of Mr. Pablo Bergés. Gentlemen, this experiment is decisive, because it demonstrates to us not only that the yellowish conglomerates which we saw in the capillaries of the portal vein are formed by the same mobile granules which one meets in the urine and in the blood of yellow-fever patients, but because it proves also the enormous resistance of these organisms which preserve all of their vitality after having remained more than three years in Canada balsam.

It is evident that Dr. Carmona, in the above account, has made two errors of inference: First, in supposing the masses of granular material in the hepatic capillaries—probably blood corpuscles changed by the fluids in which the tissue had been hardened—to be identical with the so-called zoospores in the urine. Second, in supposing that the molecular movements observed—brownian—were evidence of vital

* Since this report was written I have had an opportunity to make cultures from urine obtained, *post-mortem*, through the walls of the bladder, in a considerable number of typical cases of yellow fever, and have found that as a rule it is sterile.

activity. The latter mistake has also led him into error with reference to the resisting power of these "zoospores" to heat and to germicide agents. Thus, on page 157, he says:

The results of these last experiments are as follows: First, temperatures of 100° to 120°, which are commonly recommended for the destruction of the micro-organism of yellow fever, are totally insufficient. In order that the action of the temperature may be effective, it is necessary to raise it to 160° and maintain it for two or three hours consecutively.

The account given of the experiments referred to shows that 160° centigrade is the temperature meant, which is 60° above the boiling-point of water, or 320° Fah.

In like manner it was found that remaining for twenty-four hours in a 1 per cent. solution of bichloride of mercury did not destroy the zoospores.

Dr. Carmona has also reported his failure to stain these zoospores with the aniline colors. He says:

At the commencement of my studies I tried to color the zoospore of yellow fever, and up to the present time I have not succeeded. Tincture of iodine produces no change upon these organisms, and if the iodine solution is aqueous the zoospores preserve all their movements in it as I have already said. * * * I have not succeeded any better in coloring these organisms with the aniline colors. I should say that I have employed by preference methyl-violet B. I have submitted the zoospores to the action of this coloring matter during a shorter or longer time (from one hour to thirty-six hours) and I have never been able to color them. The zoospores retained their proper movements in these solutions and preserved their normal color. I have employed the solutions cold and at temperatures more or less elevated, in some cases boiling, and the results have always been negative.

The above account of the characters of the so-called zoospores makes it apparent that Dr. Carmona has constantly mistaken the well-known molecular or brownian movement of minute particles suspended in a fluid for vital movements, and has taken this as evidence that he had under observation living microorganisms. For us the characters given seem almost to demonstrate that the particles in question were inorganic; at least they were not micrococci, such as Dr. Carmona showed me in a mounted preparation in his laboratory, said to be from a culture obtained from the urine of a yellow fever patient, for these "zoospores" were well stained and were undoubted spherical organisms—micrococci, which in their morphology resembled those constantly found in urine which has undergone alkaline fermentation.

EXPERIMENTS UPON ANIMALS.

Dr. Carmona says on page 137 of his Mémoire:

I will speak to you later of the inoculations which I have practiced, and which I consider capable of preserving from the *vomito negro*. To-day I will confine myself to telling you that before deciding to inoculate man I made a great number of experiments upon animals. I introduced into them the zoospores by different channels. I caused it to penetrate directly in the torrent of the circulation; I deposited it in the cellular tissue; I introduced it into the respiratory passages, and into the alimentary canal, and finally I injected it into the renal parenchyma, and never, no never have I succeeded in obtaining the symptoms of yellow fever.

It appeared to me strange that the zoospore being the generative principle of yellow fever, the malady was never reproduced in the great number of experiments which I have made. To-day the explanation is very simple, since we know that neither the zoospore nor the spores which come from it develop directly in the economy the *peronospora lutea* which determines the *vomito noir*. It is necessary first that the spores germinate and give birth to the *mucédinée*, an intermediary species, in order that these spores may develop in the animal economy the tableau of symptoms called yellow fever by the development of the *peronospora lutea*.

Although Dr. Carmona has abandoned his *peronospora lutea*, his experiments with the so-called zoospores remain as evidence of the innocuousness of the micro-organisms present in the material used in his experiments, so far as the animals experimented upon are concerned—species not named. His results are in accord with those heretofore reported from other sources.

METHOD OF INOCULATION.

Dr. Carmona gives the following account of his method of inoculation:

The method of performing the inoculation is very simple. In the first place, the urine of the sick is collected, taking care not to take that of patients suffering from any visceral affection, still less from gonorrhea or syphilis. It is well to employ the urine secreted when the disease is well established, because it contains a greater quantity of zoospores. This urine is placed in large shallow plates, and abandoned to spontaneous evaporation, having care that the evaporation is complete, and that no trace of humidity remains. If the layer of residue is very thick it is well to spread it out so that it may be penetrated throughout by the oxygen of the air. By following this advice you will surely avoid the inoculation of the microbes of putrefaction. When the residue is well dried it may be used for the inoculation. I usually place 1 or 2 centigrams of the dry residue in a gram of distilled water. I triturate it in such a manner that the mixture is as perfect as possible, and charging a Pravaz syringe, I make a subcutaneous injection in the right arm.

The results are various, but no serious accident has ever occurred. I was first inoculated, September 29, 1881. I felt a lively pain at the moment of the injection and some minutes after, but it disappeared promptly to give place to a slight tumefaction without redness of the skin, which interfered somewhat with the movement of the arm. The fourth day all had disappeared, and I really had no febrile movement, since the thermometer did not go more than a few tenths above 37°; the urine became scanty and took a slightly reddish color. The malaise was insignificant and I continued my ordinary occupations.

I count, to day, nearly two hundred persons inoculated, and among them several experienced, some hours after the inoculation, a febrile movement, which sometimes caused the thermometer to mount to 38.5°. The duration of this febrile movement did not exceed twenty-four to thirty hours. The local accidents have been most varied. There was almost always tumefaction at the point of inoculation, but the extent and size of this tumefaction varied greatly. In many cases there was redness of the skin. These local phenomena lasted four or five days, but in general those inoculated continued about their ordinary affairs. Once only I have seen developed a phlegmon which terminated by suppuration.

RESULTS OF DR. CARMONA'S INOCULATIONS.

In an appendix of his "Leçons sur l'étiologie et la prophylaxie de la fièvre jaune," Dr. Carmona has given a detailed statement of his inoculations and their results, from which I shall quote with such comments as seem called for.

When my lessons upon the etiology and prophylaxis of yellow fever were already in press, together with the preface written for them by my friend Dr. Edward Liceaga, professor of operative medicine in this faculty, and president of the superior council of health, I had occasion to study upon a greater scale the effects of the protective inoculations, both because the number of persons who desired to be inoculated increased from day to day, and by reason of the invitation which I received from General Ignacio Revueltas, under-secretary to the minister of war and of the navy, to inoculate the garrison at Vera Cruz. This opportunity to study in detail the effects of protective inoculations made me decide to adjourn the publication of my "lessons" until I could give an account of the result obtained in the garrison at Vera Cruz.

I should remark that the protective inoculations were made in the last days of the month of May, 1885, precisely in the period when the epidemic of yellow fever was on the increase.

The method employed was the same that I have indicated in my "lessons." *I took the urine of patients with yellow fever and without other preparation I abandoned it to spontaneous evaporation. When the residue was entirely dry, I took a centigram of it and dissolved it in distilled water, and by means of a Pravaz syringe, I introduced this liquid into the cellular tissue on the posterior face of the left arm.*

Up to the present time, November 6, I have made one thousand three hundred and fifty-eight inoculations without including those which were made at Colima, Sinaloa, Sonora, and Oaxaca. I think it useful to make the remark that in no case has there been any serious accident as the result of the inoculations, notwithstanding the fact that the residue of the urine is formed exclusively by millions of zoospores thrown off by the patients. Besides, *I insist upon this fact, that I have never had recourse to any method of attenuation. The number of persons inoculated being already considerable, I think I am authorized to say that the zoospores penetrate without any danger into the animal economy, and consequently that it is completely useless to seek to attenuate the virus.*

I ought, however to observe that in order that the inoculation may be inoffensive *it is absolutely necessary to evaporate the urine completely, until it is perfectly dry, and to*

make the inoculations in localities which are not visited by yellow fever; or if one is obliged to make them in infected localities they should be practiced during the period of the year when the disease has not yet declared itself.

I have already mentioned in my "lessons" the possibility of producing yellow fever in cases in which the inoculations are made in the infected localities and at the time when the epidemic is developing. This doctrine which up to that time was only hypothetical has unfortunately been confirmed. In the month of May of this year when the epidemic of *vomito* commenced to develop at Vera Cruz, six prisoners were inoculated, and in two of these the local symptoms of the inoculation were followed immediately by those of grave yellow fever and both died some days after, upon the same day.

These fatal results, not having presented themselves in the one thousand three hundred and fifty-eight inoculations made in localities where yellow fever has never existed, makes us see the truth of the doctrines established in my "lessons." It must not be forgotten that in localities where yellow fever reigns and in times of epidemic a mucedine is developed either in the residue of the urine or in blood drawn from yellow-fever patients. It is necessary also to remember that observation has shown that this mucedine does not develop every year, nor in every season o the year, but that its development coincides with the appearance of epidemics of yellow fever. *So long as this mucedine does not develop there is no yellow fever, and as soon as yellow fever appears the same mucedine develops as well in the sediment of the urine as in the blood of the sick.*"

Remarks.—As Dr. Carmona has abandoned the "mucedine" as an etiological factor in the production of yellow fever it is unnecessary to enter upon a critical discussion of the above-quoted explanation of a fact which appears to us to admit of a very simple explanation. Six prisoners living in an infected locality were inoculated by Dr. Carmona's method; two of the six fell sick with yellow fever soon after the inoculation and died. One thousand three hundred and fifty-eight persons inoculated outside the infected area did not suffer an attack of yellow fever as a result of the inoculations made, nor did four of the six prisoners referred to. Evidently the fact that two inoculated prisoners living in an infected area fell sick and died from the prevailing sickness can not properly be ascribed to the inoculation practiced, unless it be that this may have acted as a secondary cause—just as inebriation, excessive fatigue, etc., may act in presence of the essential and specific first cause to develop an attack of this and other infectious diseases. On the other hand the two cases furnish evidence which is not favorable to the supposed protective power of the inoculations practiced.

After having demonstrated the perfect innocuity of the preventive inoculations, made according to the rules which I have recommended and after having made known the dangers of making them in the localities infected by the *vomito*, above all when it reigns as an epidemic, let us pass to the study of the results obtained, and to make known the degree of confidence that we may have in considering them as a means of prophylaxis against yellow fever.

The first two hundred and eight preventive inoculations that I practiced were made with the zoospores of a urine which I had preserved since the year 1881. This residue, which it may be said in passing is very arid of atmospheric moisture, had become liquid several times and had again become dry. The zoospores which existed in it were endowed with very free movements, and when we put a small quantity in a drop of water they became intimately mingled with this fluid and only a small number remained in conglomerates.

This residue served me to inoculate all the persons upon whom I practiced this operation up to the 3d of January, 1885. Very well, none of these individuals was attacked by yellow fever, notwithstanding that all were exposed for a longer or shorter time to the action of the morbific principle, and that many of them have already passed through several epidemics of yellow fever, some in Havana, others at Vera Cruz, Mazatlan, Colima, in Lower California, etc.

M. Joaquin del Villar and a civil engineer experienced at Mazatlan symptoms so benign that they scarcely attracted attention. M. del Villar, who after twenty-four hours of malaise had a slightly yellow tint, only gave up his daily occupations for a single day.

I wish to speak of some particular facts because they may serve to make known the value of the prophylactic method. More than one hundred persons were sent by the Government to the Universal Exposition at New Orleans, who were inoculated with the residue of the urine of which I have spoken, and notwithstanding the fact that they remained in this city after the appearance of yellow fever none of them were attacked.

We remark here that yellow fever did not prevail in the city of New Orleans during the year of the Universal Exposition, and that thousands of unacclimated persons from various parts of Europe and from the northern portion of our own country visited New Orleans during the Exposition without contracting yellow fever, although they had not been inoculated by the method proposed by Dr. Carmona.

On the seventh, eighth, and ninth of November, 1887, I inoculated thirty-eight persons of an opera bouffe company which was on its way to Vera Cruz and to Havana in order to give theatrical representations. The *vomito* reigned in these two cities, and notwithstanding their own avowal that they had given themselves up to all sorts of excesses none of these artists were attacked with yellow fever.

With reference to these thirty-eight persons we would remark that as they visited the cities of Vera Cruz and Havana during the winter season—that is to say, soon after their inoculation on the 7th, 8th, and 9th of November—they were not exposed to any test worthy of consideration. Strangers are in the habit of visiting these infected cities during the winter months, and they do so with impunity. We therefore find no evidence thus far of the protective value of the inoculations practiced.

At the commencement of the year 1884 ten persons from Mexico set out for Mazatlan for the purpose of establishing themselves there. Four of them were inoculated, and none of these were attacked with yellow fever; the six others who did not take the same precaution were successively attacked and all died.

This seems more like evidence of protective value; but in the absence of exact data as to the exposure of the ten persons after their arrival—that is to say, whether it was identical in all the cases of those inoculated and those not inoculated—and in the absence of a nominal list and verification of the alleged facts by some one on the spot, we can not give great weight to this evidence.

From the 4th of January to the middle of June of the present year I have inoculated five hundred and thirty-two persons, and these inoculations were made with the residue of urine which had been dried without being subjected to alterations of moisture and dryness such as the residue first used had suffered. I insist upon this detail for reasons which I will explain later.

Among the five hundred and thirty-two inoculated were three hundred and sixty-two soldiers who composed the garrison of Vera Cruz, two hundred and eighteen more who had been inoculated by me in Mexico the 10th of May, making a total of three hundred and eighty who, not having been born in the locality and not having had yellow fever, were exposed to the contagion of the epidemic which commenced to develop. This group formed of three hundred and eighty soldiers of the garrison of Vera Cruz is the more important for our study: First, because they were inoculated when the epidemic of Vera Cruz commenced to develop and because they were obliged to pass through it at the said port; second, because their number was considerable and they lived in the same hygienic conditions, and as they could constantly be observed the results ought necessarily to be more certain; and third, because one could establish a comparison between this group of inoculated persons and the convicts who were not. It must be remembered that the epidemics of yellow fever at Vera Cruz when they attain a certain degree of intensity, as that which has just passed, make great ravages among the soldiers, and it is not rare to see in such conditions that the half or the third of the garrison is attacked. There have even been cases, in years when the epidemic was very severe, when an entire battalion has been attacked.

I ought also to state that the figures I am about to give are all those which have been received officially by the minister of war, and that the information has been collected at Vera Cruz by physicians who have not shown themselves to be partisans of the doctrine of inoculation. Besides, I have never disputed the diagnosis, and having confidence in the loyalty and good faith of my confréres, I have accepted without hesitation all the cases of yellow fever which they have judged as such.

I will mention by name the persons attacked, because I wish that every one may be convinced that I do not conceal any misfortune, being persuaded, as I am, that to deceive others would be to wish to deceive one's self, and that in matters of observation deception could not last for a long time. The table No. 1 shows the sanitary condition of Vera Cruz (so far as yellow fever is concerned) before the inoculations were made.

TABLE No. 1.

	January.		February.		March.		April.		May.	
	Admitted.	Died.	Admitted.	Died.	Admitted.	Died.	Admitted.	Died.	Admitted.	Died.
Military hospital	12	4	4	3	6	5	4	4	31	15
Civil hospital, San Sebastian	0	0	0	0	0	0	0	0	6	1
Civil hospital, Loreto	1	1	0	0	0	0	2	2	2	0
Total	13	5	4	3	6	5	6	6	39	16

The month of May, during which the epidemic commenced to augment, was the moment chosen to make the inoculations at Orizaba. We must remark that the troops commenced to go up after the 19th of the same month in little groups, going away in this manner from the infected locality. The inoculations terminated the 31st of May, except a group of artillerymen, who were inoculated June 5, and another on the 12th of the same month.

However small the number of days during which each group was separated from the infected locality, it is evident that the number attacked in the month of May was always less than it would have been if their stay in Vera Cruz had been permanent; considering above all that the inoculations lasted twelve days, which is nearly equal to half a month. I insist upon this circumstance, because we are going to establish a comparison between the number attacked during the month of May among the soldiers of the garrison and the non-acclimated prisoners—*forçats*.

Of the thirty-one admitted to the military hospital during the month of May, sixteen were prisoners and fifteen soldiers; but two of the latter were attacked at Orizaba, having carried the germ from Vera Cruz. So that in the month of May there were seventeen soldiers attacked and sixteen prisoners. It is almost certain that if the troop had not removed from Vera Cruz there would have been a greater number of sick. At the end of May there remained one hundred and seventy-three *forçats* not inoculated and not acclimated, who will be compared with three hundred and eighty soldiers, not acclimated, but already inoculated. The proportion is then 2.2 of the second for 1 of the first.

The epidemic had little intensity during the first four months of the year, but already in the month of May eight cases had been admitted to the civil hospitals, and as we will see further on the epidemic became more intense during the following months.

Table No. 2 shows the number attacked and the deaths during the entire epidemic, explaining with care the number inoculated.

TABLE No. 2.

1885.	Military hospital.				San Sebastian.		Loreto.		City.
	Prisoners.		Inoculated soldiers.						
	Admitted.	Died.	Admitted.	Died.	Admitted.	Died.	Admitted.	Died.	Died.
June	18	8	5	3	13	6	8	3	6
July	18	13	11	6	58	36	16	6	20
August	19	.....	10	8	41	29	9	6	30
September	9	.....	0	0	.....	10	.....	5	10
October	8	.....	0	0	.....	.....	.....	.....	.....

In studying this table we see at once that of the one hundred and seventy-three prisoners not inoculated, seventy-two were attacked during the five months in which the epidemic was most intense; that is to say a little less than 42 per cent., while of the three hundred and eighty soldiers inoculated only twenty-six were attacked, or a little less than 7 per cent. We see, also, that in the months of September and October there were no cases in the last group, although the epidemic continued with considerable force.

At the end of the month of July one hundred and seventy-four soldiers, not inoculated, for the most part coming from Tabasco, arrived in Vera Cruz; these were immediately influenced in a most intense manner, so that in the month of August seventeen of these soldiers were attacked by yellow fever; in adding these seventeen to the nineteen prisoners (forçats) and the ten inoculated, we have in all forty-six attacked; the total number admitted to the military hospital. In the month of September there were twenty-one attacked among the newly-arrived soldiers, which, added to the nine prisoners noted in Table No. 2, makes a total of thirty admitted, the number in the military hospital in the said month of September. In October there were eight prisoners attacked and eighteen of the newly-arrived soldiers, making a total of twenty-six admitted. *In September and in October none of the inoculated were attacked with yellow fever.*

It has not been possible for me to ascertain the number of prisoners who died in the months of August, September, and October, because in the documents received the total number of deaths among the non-inoculated soldiers and prisoners is given for the different months, but without mentioning the respective number of each. In the month of August there were twelve deaths among the prisoners and soldiers not inoculated, which, united to the eight inoculated who died, makes a total of twenty deaths for the month of August. In the month of September twenty-three persons died among the prisoners and soldiers not inoculated, but I do not know what was the number of the former and what of the latter. In October there were thirteen deaths out of twenty-six admitted.

From all these facts it results, first, that of the three hundred and eighty inoculated there were twenty-six attacked and seventeen died in the months of June, July, and August; second, that in September and October none of the inoculated were attacked, notwithstanding that the epidemic struck a good number of victims among the non-inoculated.

If we compare these results with those among the non-inoculated prisoners we will see that, having had among them seventy-two attacked, it is easy to establish a proportion, saying that if one hundred and seventy-three gave seventy-two cases, how many should three hundred and eighty give? The number of attacked should have been one hundred and fifty-eight; there were only twenty-six. It follows that the inoculation prevented one hundred and thirty-two cases of yellow fever, of such a gravity that nearly 50 per cent. of the sick died.

A comparison of the mortality among these prisoners with that of a group of soldiers living in comfortable barracks and under much more favorable hygienic conditions appears to me to be without any scientific value, and the same may be said with reference to the comparison of the soldiers who were inoculated in the month of May and among whom twenty-six cases and seventeen deaths are said to have occurred, with the one hundred and seventy-four non-inoculated soldiers who came to the city the end of July. We are not informed how long the soldiers composing the garrison of Vera Cruz had been stationed in that city prior to the date upon which they were inoculated, and how many "acclimated" men were included in the number given; on the other hand, the one hundred and seventy-four soldiers, not inoculated, who arrived the end of July, are stated to have come, for the most part, from Tabasco, a town in the interior. The fact that the original garrison of Vera Cruz, inoculated in May, after losing seventeen men out of twenty-six attacked with yellow fever during the months of June, July, and August, should have sustained no further losses in September and October seems to me quite in accordance with what often occurs under similar circumstances, and the considerable losses during these months occurring in a newly-arrived detachment also corresponds with what has frequently occurred in other localities, where, after the termination of an epidemic as a result of the exhaustion of susceptible material, a new outbreak follows the arrival of unacclimated persons.

Moreover, Dr. Carmona states on the following page of his memoir that during the month of May, before the inoculations were practiced, there had been seventeen cases and eight deaths from yellow fever in the garrison, so that the three hundred and eighty inoculated had already been exposed without contracting the disease, and were in fact persons who had shown a certain insusceptibility in presence of the malady; that is to say, they were the survivors of a larger number which had already suffered a considerable loss.

Of all the figures given by Dr. Carmona, the most important for us, as bearing

upon the prophylactic value of his method of inoculation are those which inform us that twenty-six of those inoculated were seized with yellow fever, and that seventeen of these died. Dr. Carmona's confrères in Vera Cruz seem to have taken the same view of the case, for so far as I could learn they were not convinced of the value of the method, and it has not been practiced in Vera Cruz since the date of the above-mentioned experiment upon the military garrison of the city.

Dr. Carmona has attempted to account for the mortality among those inoculated at Vera Cruz by supposing that "some of those inoculated may not have received a sufficient quantity of the microbes for the perfect saturation of the economy." He says:

When in the month of June I learned that some of my inoculated were attacked with yellow fever, I asked myself if the want of success was not, perhaps, due to the fact that by the simple evaporation of the urine the albumen remaining in the residue conglomerated the zoospores, rendering them heavy and but slightly mobile. In this condition it might well be that some of those inoculated had not received a sufficient quantity of microbes for the perfect saturation of the economy just at that time. I was to inoculate seventy-eight soldiers who were about to set out for Acayucan, and I resolved to control the results of the inoculations made with the residue, such as I had prepared up to that time, and for this purpose I had the seventy-eight soldiers inoculated by Dr. Mondragon with preparations similar to those which we had employed in the inoculations made at Orizaba. Four days after we studied with the microscope the blood of some of these soldiers, and we found that the quantity of zoospores was the greater when the person had received the last portions of the virulent liquid. Thus, in the blood of the first inoculated one saw scarcely any zoospores, while in that of the last there was a considerable quantity.

The result of this experiment shows that the twenty-six unsuccessful cases were probably due to the fact that all of the soldiers inoculated have not received the quantity of zoospores necessary to saturate the economy, and consequently that it is necessary to stir the virulent liquid before each inoculation, or to remove the albumen by heat or by alcohol before evaporating the urine.

Knowing that the zoospores are not altered either by alcohol or by the temperature which coagulates albumen, I have not hesitated to submit the urine to a temperature of 76°, and after cooling I filtered it and left it to spontaneous evaporation. By this proceeding one loses, without doubt, some microbes which remain attached to the albuminous precipitate, but in compensation those which we obtain have a great mobility, and but few conglomerations remain.

Remark.—Extended experiments made by the writer * show that the vitality of micrococci, such as Dr. Carmona showed to me in his laboratory as zoospores, and such as were present in the culture which he kindly gave me, are destroyed by a temperature much lower than that above mentioned, and I have proved by direct experiment that a temperature of 60° C., maintained for ten minutes, serilizes Dr. Carmona's cultures so far as micrococci are concerned. I must therefore regard the above procedure as fatal to his so-called zoospores, and can not accept his explanation of the subsequent exemption from attack which the seventy-eight soldiers inoculated with this material are said to have enjoyed. Dr. Carmona says:

With the zoospores obtained by the new method I reinoculated seventy-eight soldiers, who were to set out for Acayucan, and I recommended that the liquids should be more charged with zoospores. Of these seventy-eight soldiers, two remained in Mexico and seventy-six went to Vera Cruz in the month of July on their way to Acayucan. One, Francisco Gonzalez, who set out without being inoculated, joined the seventy-six inoculated. They remained in Vera Cruz six days, and notwithstanding that during this month the epidemic was very severe, and notwithstanding that these soldiers descended to the coast for the first time, none of them were attacked with the *vomito*. One died of peritonitis, according to what Dr. Palazuelos has written me. Upon their arrival in Acayucan, Francisco Gonzalez, the only one not inoculated, fell sick with the *vomito* and died a few days after. All the others remained in perfect health.

Remarks.—The facts as above stated seem to support Dr. Carmona's claims as to the protective value of his inoculations, although the time during which the men re-

* The thermal death-point of pathogenic organisms. Am. Journal of the Medical Sciences, July, 1887.

mained in Vera Cruz was rather short for a satisfactory test and we are not informed where they remained and can not form a judgment as to the real exposure to which they were subjected. In view of all that has been said thus far, and in the absence of any precise information other than that contained in the above quoted extract, I must still retain my position of scientific skepticism with reference to the protective value of Dr. Carmona's inoculations. Indeed, Dr. Carmona himself very frankly admits, in closing his account of the laudable attempt which he has made to demonstrate by experiment the value of his method, that the demonstration is not sufficient to comply with the exactions of science. He says:

I do not suppose that what has been done up to the present time is sufficient in order that the method of prophylaxis which I propose may be admitted in a definitive manner by science; but I believe that the results are sufficiently significant to animate practitioners, so that statistics upon a greater scale may be obtained to decide the question. If my doctrines are realized I shall consider myself very happy to have furnished to humanity the means of avoiding one of the most terrible scourges which has ever afflicted it.

CONCLUSIONS.

Facts relating to the endemic and epidemic prevalence of yellow fever, considered in connection with the present state of knowledge concerning the etiology of other infectious diseases, justify the belief that yellow fever is due to a living micro-organism capable of development under favorable local and meteorological conditions, external to the human body, and of establishing new centers of infection when transported to distant localities.

Inasmuch as a single attack of yellow-fever, however mild, protects as a rule from future attacks there is reason to hope that similar protection would result if a method could be discovered of inducing a mild attack of the disease by inoculation, or otherwise.

The hypothetical yellow-fever germ, multiplying external to the human body in unsanitary places in tropical regions where the disease is endemic, or during the summer months in the area of its occasional epidemic prevalence, establishes infected localities, and susceptible persons contract yellow-fever by exposure in these infected areas. We infer, therefore, *a priori*, that the yellow-fever germ invades the system by the respiratory tract, by the alimentary canal, or from the general surface of the body, and it should be found in the blood and tissues, or in the alimentary canal, or upon the surface.

Another possibility presents itself, viz, that the germ multiplying in unsanitary localities external to the body produces a volatile poison which contaminates the air, and that an attack is induced by the toxic effects of this potent chemical poison. The more or less prolonged period of incubation—two to five days—in numerous cases in which the attack has been developed after removal from the infected locality is opposed to this latter hypothesis.

In the light of what is known of the etiology of other infectious diseases, the hypothesis that the germ really finds entrance to the body of the person attacked and multiplies within it is that which presents itself as most probable, and it hardly seems worth while to consider any other, unless this is proved by a complete investigation not to be true.

Naturally the attention of investigators has first been given to a search for the "germ" in the blood of those attacked and in the blood and tissues of the victims of the malady.

The researches made up to the present time have failed to demonstrate the constant presence of any micro-organism in the blood and tissues of those attacked.

My own researches, recorded in the foregoing report, show that no such micro-organism as Dr. Domingos Freire, of Brazil, has described in his published works, or as he presented to me as his yellow-fever germ at the time of my visit to Brazil, is found, as he asserts, in the

blood and tissues of typical cases of yellow fever. There is no satisfactory evidence that the method of inoculation practiced by Dr. Domingos Freire has any prophylactic value.*

The claims of Dr. Carmona y Valle, of Mexico, to have discovered the specific cause of yellow fever have likewise no scientific basis, and he has failed to demonstrate the protective value of his proposed method of prophylaxis.

It is highly important, in the interest of science and of the public health, that further investigations be made by more exact methods, which have been perfected since Drs. Freire and Carmona made their researches, and with which they were evidently not familiar.

The failure thus far to find a specific micro-organism in the blood or tissues makes it desirable that a thorough research should be made with reference to the micro-organisms present in the alimentary canal, for it is possible that in yellow fever, as in cholera, the disease is induced by a micro-organism which multiplies in this situation. Additional researches are also required before we can say definitely that there is no germ demonstrable in the blood and tissues. Having exhausted our resources by the method of direct examination, and by cultures from blood drawn during life, it is highly desirable that various culture media should be inoculated with material taken, with proper precautions, from the various organs, at the earliest possible moment after death. †

POST SCRIPTUM.

BALTIMORE, *September* 23, 1889.

In his attempt to neutralize the force of my evidence and to establish his claim to have discovered the specific microbe of yellow fever, Dr. Domingos Freire has referred to the observations of Babes, of Finlay and Delgado, of Gererd and of Rangé as confirming his own. As a matter of fact the observations of the gentlemen referred to give no support whatever to this claim, inasmuch as none of them have described anything corresponding with the "*Cryptococcus xanthogenicus*," or even with the micrococcus which he presented to me as his yellow-fever germ.

Thus the micro organism found by Babes in material sent to him from Dr. Lacerda's laboratory in Rio de Janeiro is a short bacillus, arranged in chains, and not a micrococcus (see fig. 3, p. 173, and compare fig 1, p. 160). Babes himself has reported his failure to find this bacillus in material from other sources, and his researches show the absence of Freire's micrococcus in the material examined by him, as this is easily stained by the aniline colors, and if present could not have escaped the observation of so accomplished a microscopist and bacteriologist. In the second edition of "Les Bactéries" Babes says:

Since these researches we have had the opportunity to examine several series of sections from yellow fever. First, the liver and kidney of two individuals dead from

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* NOTE.—My more recent researches made in Havana in 1888 (ten autopsies), and in 1889 (thirty autopsies), fully confirm this conclusion.

BALTIMORE, *September* 21, 1889.

† The writer went to Brazil and to Mexico fully prepared to make the experiments indicated, but, unfortunately, was not able to secure any autopsies in either place, and the limit as to time fixed by his orders made it necessary for him to return to the United States without having made these important researches.

Since the above was written I have made extensive researches of the kind indicated, having made ten autopsies in typical cases in the military hospital in Havana in the summer of 1888, three autopsies during the epidemic at Decatur, Ala., in the autumn of the same year, and thirty autopsies in Havana during the summer of the present year (1889). The results of these investigations will be recorded in detail in a report to be submitted hereafter.

SEPTEMBER 1, 1889.

this malady, collected by Dr. Alvarez, were examined in the Laboratory of Pathological Anatomy of the Faculty of Paris, without any bacteria having been found; second, material from three cases of yellow fever which Koch was kind enough to confide to one of us. In these last three cases, notwithstanding the most scrupulous research, and notwithstanding the advice of Koch, it was impossible to find the little chains in the brain, the kidneys, the liver, and the spleen. We must suppose, then, that in yellow fever, as in other infectious maladies, microbes are only found in the parenchymatons organs in certain cases, and not in all. The question whether these micro-organisms really constitute the cause of the malady, or simply a complication, is consequently not resolved.

The extended researches of my friend, Dr. Carlos Finlay, of Havana, also give no support to Freire's claims, inasmuch as the micrococcus in tetrads, which has especially engaged his attention, and which for a time he believed to be the specific etiological agent in the disease under consideration, is entirely distinct from the micrococcus of Freire. Finlay's *micrococcus tetragenus febris flava*, which I have called *micrococcus tetragenus versitilis*, a name which he accepts, is a large coccus in tetrads, which differs essentially, both in its morphology and in its growth in culture media, from the micrococcus of Freire. This I can assert most positively, as I have had authentic cultures of each, given me by the gentlemen themselves, under continuous observation for nearly two years.

Moreover, I have made extended culture experiments in Havana during the past two years, which show conclusively that neither of these micrococci is present in the blood of yellow-fever cadavers, withdrawn from the heart or the liver shortly after death. In one case only out of thirty-five autopsies in which I have made cultures from the liver, I have obtained the "tetragenus" of Finlay, and I have not encountered the micrococcus of Fréire in a single instance. On the other hand, I have obtained both of these cocci in cultures from the surface of the body of patients in the hospitals of Havana, and the "tetragenus" is one of the most common micro-organisms encountered in such cultures, whether made from the surface of yellow-fever patients or those suffering from other diseases.

With reference to the observations of Gererd it is evident from his own account that if he encountered micrococci they were associated with spore-forming filamentous bacilli, and that he was entirely unfamiliar with this class of micro-organisms. As he is not known as a bacteriologist and has not given a detailed account of his methods of research, no scientific value can be attached to his observations. In a translation of his report made by Dr. Wolfred Nelson and published in the Canada Medical Record of July, 1886, I find the following account of the morphology of the micro-organisms encountered by him:

In the month of June, 1882, in a report to the superior agent of the Interoceanic Canal Company, resident in the city of Panama, South America, I had the honor to inform him that I had found in the blood of yellow-fever patients some microscopic organisms—some filiform, others resembling a string of beads (*chaplets*), and, lastly, brilliant little bodies. That the organisms were constant in appearance, and could thus serve as elements for diagnosis.

After some trials and a great many failures I succeeded in isolating the microbes, and obtained them in great quantity without the human body by artificial cultivation, in liquids suitable for their nutrition and reproduction.

I was then enabled to study the mode of existence of the microbes. If one observes the filiform bodies attentively for a given time he perceives in their transparent and homogeneous substance a series of small corpuscles that reflect light more than the other parts of the microbe. Little by little these corpuscles arrange themselves around a central axis or core, giving the organism the appearance of a string of beads, *chaplet*. (This French word signifies the string of beads "told" by devout Catholics while praying.) Soon other changes follow, the string-like formation separates, and in place thereof nothing remains but a mass of brilliant little points. The size of the little points is about the thousandth of a millimeter. These corpuscle germs have great resistance. *They do not perish by drying, and can after many years serve to propagate the disease by regenerating the filiform bodies when placed under favorable conditions.*

Compare this with Dr. Fréire's account of the morphology and mode of development of his *Cryptococcus xantrogenicus*. In his principal work, published in 1885, he says:

When we follow with care and attention the march of the development which characterizes the germs which produce yellow fever, we acquire a certainty that, com-

mencing to present themselves under the form of little points almost imperceptible, they afterward gradually increase in diameter until they attain considerable dimensions; so that the little beings, which at the outset had the appearance of little grains of sand, not measuring more than 0.001 millimeter to 0.002 millimetre in diameter, arrive little by little to such a development that they reach the dimensions of 0.005, 0.007, 0.008 millimeter, and sometimes even more in certain conditions. When they have attained the adult age these cells are broken at divers points and discharge their contents, composed of spores already formed, mixed with a viscous substance of a yellow color, composed of a pigment and protoplasmic substance, and of the liquids elaborated by the cells.

In an address delivered in Paris in 1887 Dr. Freire repeats this account of the mode of development of his cryptococcus. He says:

Each adult cell is ruptured at one or several points, and allows to escape its contents, composed of germs which are to perpetuate the species, and two pigments—one yellow, destined to infiltrate the tissues and to produce the icteric color which has given name to the malady; the other black, insoluble, etc.

Dr. Rangé, a medical officer of the French navy, whose researches have been repeatedly referred to by Dr. Freire as confirming his own, says in his report:

Unfortunately for our researches we did not possess high powers. I could not exceed 540 diameters, and I had no coloring matters for isolating the microbe in the blood, according to the method of Ehrlich; therefore I only give these details with reserve. The figured elements which we have drawn were met with in the black vomit of man, the contents of the stomach of guinea-pigs, in the cultures of blood and in condensed watery vapor, but in less number. They are agglomerations of cells, some round with a central nucleus; beside these, and with a more considerable development, we met with elliptical cells having the dimensions of a blood globule, and with a nucleus near one of the extremities of the greater diameter. These cells were found in groups of two or three, joined by the extremity containing the nucleus. This approached the periphery little by little; at this moment one observed a slight swelling, a sort of bud, which separated from the cell which had given it birth. Beside these elements, one finds others in the form of rods, large and short, not branched. These bacilli sometimes contain granules. We believe that they come from the elliptical cells, for we have followed under the microscope the phases of their transformation. But the absence of a didactic treatise, the absolute absence of bibliographic resources prevents us from making any positive affirmations with reference to these micro-organisms.

Notwithstanding the very just conclusion above reached, Dr. Rangé, at the end of his memoir, says:

In uniting these various results, shall we conclude that there is *a bacillus* of yellow fever, bacillus icteroid, and that it is possible to find a vaccine? We believe it without affirming it.

The above quotations will suffice to show any well-informed bacteriologist that the claim of Dr. Freire does not receive any support from the observations of the gentlemen mentioned, whereas several competent bacteriologists have reported their failure to find his "cryptococcus" or any other micro-organism in the blood.

Dr. Paul Gibier, who went to Havana in the expectation of finding what Freire had described, made researches by approved bacteriological methods and reports an entirely negative result. In a communication to the French Academy of Sciences he says:

HAVANA, *January* 22, 1888.

At the commencement of the year 1887 Dr. Domingos Freire, professor in the faculty of medicine of Rio de Janeiro, came to Paris in order to present to the scientific public his studies upon yellow fever. M. Freire was presented to me by Dr. Rebourgeon, who had studied this malady with him in Brazil. The laboratory of comparative pathology of the museum was opened to these *savants*, who resumed the experiments the results of which had previously been published by M. Freire. I was requested by M. Freire to examine the cultures which he had brought with him and to treat them by the new bacteriological methods which had not yet been applied in his researches. After these investigations, made in common, M. Freire had the kindness to associate me in a communication which he made in his own name and that of Rebourgeon to the Academy of Sciences during the month of March, 1887.

Since, and as a result of this communication, I received from the minister of public instruction the mission to go and "study yellow fever in the countries where it pre-

vails habitually, and the prophylactic measures which may be opposed to this malady." In the early part of November, 1887, I disembarked at Havana, where the yellow fever still shows itself at this epoque in the so-called *sporadic* form.

I give as succinctly as possible the results of my first investigations, which were made in the hospitals of Havana.

November 16.—Among several cases of yellow fever I chose that one which appeared to me to be the most grave, in order to collect blood and urine. Fifth day of sickness: Fever, albuminuria, black vomit, etc. Fatal case.

November 17.—In an autopsy practiced about eight hours after death, I collected blood from the left ventricle and from the right auricle. * * *

November 27.—Among several cases examined I collected, from the most severe, blood and black vomit. Fatal case.

December 14.—Case in fourth day of the disease: Albuminuria; collected blood, urine, and black vomit. Recovered.

December 22.—Clinical examination of a severe case: Abundant black vomit, buccal hemorrhage, etc.; 23d, autopsy of this case *made two hours after death*; collected blood from the heart. * * *

In order to avoid useless repetition I will detail in a general way the methods pursued in the examination of the liquids collected, with the precautions usual in bacteriological researches.

In each case several preparations of blood were examined in a fresh condition, then dried and stained; the same method was pursued with the urine and the black vomit.

Inoculations, by numerous punctures, were made in agar-agar jelly with blood, urine, bile, and serum from the pericardium. * * * Numerous thin sections of the various organs were also made; these were stained with a view to demonstrating the presence of microbes.

Results obtained.—I am obliged to confess here, however much it may cost me, that my results contradict in an absolute manner the facts advanced by M. Domingos Freire, from whom I have the regret, as well as the duty, to separate myself.

The blood.—In a great number of preparations, fresh or colored, it has been impossible for me to verify the presence of micro-organisms. The cultures, repeated a great number of times, remained sterile.

The urine, treated in the same manner as the blood, has constantly given a negative result.

The pericardial liquid and the bile, like the blood and urine, did not contain micro-organisms. I have found that even in the gravest cases seen by me the blood examined by the microscope did not present any appreciable trace of alteration of its elements.

The numerous sections which I have made of the different viscera also have failed to show me the presence of microbes.

Dr. D. Tomayo, of the bacteriological laboratory of the "Crónica Médico-Quirurgica," of Havana, has also reported a negative result in his repeated examinations of blood drawn from the finger during life. His evidence is valuable both because he is a competent and conservative bacteriologist, having been instructed in the methods of research in Pasteur's laboratory in Paris, and also because he gives a detailed account of his method of collecting blood, which shows that he took extraordinary precautions to prevent accidental contamination of his cultures.

We quote from his paper published in 1888 as follows:

Analysis of the blood in yellow fever.—In collecting blood we have pursued the following technique: We have carefully washed the finger with soap and water; after that we have passed it through a hole made in a piece of impermeable linen a foot square; we have then washed the finger with ordinary alcohol, and afterwards with a solution of bichloride of mercury, and finally with a mixture of ether and absolute alcohol. We have also washed the isolating linen with a solution of bichloride and have covered it with a layer of glycerine; this done we isolated the finger in a little glass tube, "*cloche de cristal,*" which had been washed with the sublimate solution and well heated. By this complicated technique we have endeavored to thoroughly cleanse the skin, to remove all grease and every microbe which might be in its folds and furrows, and thus to avoid infection by atmospheric germs. Then we sterilized a lancet in the flame of an alcohol lamp, punctured the skin, and allowed the first drop of blood which presented itself to escape, using only those drops which came later, and that at the moment of their appearance. Following this proceeding we have made *ensemencements* either with the platinum needle or with sterilized pipettes in agar-agar jelly, in peptonized gelatine, and in bouillon; we have also examined the blood collected in this way, in the artificial serum of Malassey, filtered and sterilized, and lastly dried by the method of Koch. The patients from whom we obtained blood were in

the third and the sixth day of the disease; in another case the blood was collected at the moment of death. Up to the present time the cultures in agar-agar, in gelatine, and in bouillon contained in Pasteur flasks have remained sterile. * * *

THE MICROCOCCUS TETRAGENUS FEBRIS FLAVÆ OF DRS. FINLAY AND DELGADO.

My friend Dr. Carlos Finlay, of Havana, is a most enthusiastic and industrious investigator, but like many other pioneers in bacteriological research at a distance from the centers where the modern exact methods had their origin, at the time of making his first publications he was not familiar with the methods of isolating and differentiating micro-organisms, and fell into the usual and almost inevitable errors of inference as to the source and genetic relations of the various micro-organisms encountered by him in his earlier researches. He has since made himself familiar with the methods referred to and no longer insists upon the etiological relation of this micrococcus to the disease under consideration. I give below a letter received from him shortly before my departure from Havana:

HAVANA, *August* 29, 1889.

MY DEAR DOCTOR: I send you a copy of the résumé of our investigations during the year, May, 1888–'89, which Dr. Delgado and myself presented at the beginning of the year. You will see that we did not claim to have *demonstrated* that our "tetragenus" was the actual germ of yellow fever, but merely that in our recent investigations carried out with methods which we deemed to be reliable, we had again found the same micro-organism in yellow-fever finger blood and in blister serum, and also in cadaveric products of two yellow-fever autopsies. We likewise expressed the hope that you would undertake comparative experiments in order to determine, first, whether it was a fact that by the culture methods which we had described our tetragenus could be demonstrated in most of the products collected during life from yellow fever patients; and, second, whether that micro-organism is exclusively found in such patients.

I am aware that the results of three samples of yellow fever blister serum and seven samples of blister serum from acclimated subjects have given a negative answer on the second point. Yet I can not wholly divest myself of the suspicion that the greater frequency with which we have found the tetragenus in our yellow-fever cultures (from material collected during life) may have some significance, even admitting, as I do, that before any etiological importance could be claimed for it, quite a number of serious objections would have to be encountered, besides showing that it is not to be found in localities where yellow fever is unknown.

I remain, my dear doctor, yours very faithfully,

CARLOS FINLAY.

Dr. G. M. STERNBERG, U. S. Army, *Havana.*

As already stated, I have found this "tetragenus" of Drs. Finlay and Delgado to be one of the most common micro-organisms upon the surface of the body of patients in hospital, with various diseases, in Vera Cruz and in Havana. I also obtained it in specimens of blister serum collected by Drs. Finlay and Delgado from a case of brain disease, and from a case of skin disease, both of which cases were isolated from any association with yellow fever patients. The blister serum was collected from these cases and brought to my laboratory for the purpose of making a comparative research. I also frequently encountered colonies of the "tetragenus" in my laboratory in Esmarch tubes which had been inoculated with pure cultures of other micro-organisms, showing that it is quite a common atmospheric "germ" in the city of Havana.

In a recent report made by Asst. Surg. J. J. Kinyoun to the Supervising Surgeon-General of the Marine-Hospital Service he states:

The micro-organism described by Dr. Carlos Finlay (vide London Lancet, September 1, 1887), has been under observation during the past year.

Experiments made upon various animals gave no results. Later, while the observations on malarial fever were under way, this organism was discovered upon the skin of a majority of the patients suffering from malarial fevers, the patients hailing from Portland, Me., to Vera Cruz, Mexico.

THE CHARGES OF DR. DOMINGOS FREIRE.

In an address delivered before the College of Physicians of Philadelphia, and published in the Medical News of April 28, 1889, the writer gave a summary statement of

the results of his investigations in Brazil and in Mexico. In a pamphlet published in Rio de Janeiro during the present year and widely distributed by the author, Dr. Freire has made a desperate effort to sustain his previous claims and to neutralize my evidence by a virulent personal attack.

Dr. Freire's brochure referred to is divided into two portions, a "*partie technique*" and a "*partie morale.*" So far as the "*partie technique*" is concerned, I must leave the reader of the foregoing report and of Dr. Freire's publications to judge for himself of the value of the evidence presented, but I will as briefly as possible answer the charges made in the "*partie morale.*" Dr. Freire, says:

When Dr. Sternberg arrived in Rio Janeiro I was in Paris. I had not left any one as my substitute in my absence, and there was no official commission in existence occupied with my experiments. What should he do in such a case in order that his conduct might be correct? He should have awaited my return, so much the more as every one knew by the news given in the newspapers that I would return to Brazil without delay. The most elementary politeness imposed upon him at least the duty of sending me a letter or a telegram, making known to me his arrival, and urging my return. He has done nothing of the kind.

I would simply say in reply to this that having been informed that Dr. Freire was about to return to Brazil, it did not occur to me that I was called upon to address him a letter or telegram announcing my arrival. And as I had no time to lose in waiting for his return, inasmuch as my orders required me to complete my investigations in Brazil and in Mexico by the 1st of October, I at once commenced the researches with which I was charged, devoting myself especially to inquiries among the physicians practicing in Rio and to personal researches in the localities where Dr. Freire's inoculations had been practiced. I may also remark here that my visit to Rio during the non-epidemic season was not a matter of choice, but was in obedience to my orders (see p. ——). I was not consulted with reference to the date of my departure, or the length of time I might consider necessary to complete the investigation with which I was charged; and, as an officer of the Army, I had nothing to do but to obey the orders signed by the President of the United States to the best of my ability and without question.

Dr. Freire goes on to say:

On the contrary, his first care was to put himself upon intimate relations with my declared enemy, Dr. Araujo Góes, whom he refers to in his report as his friend. * * *

As I have stated in the introduction to my report, upon my arrival in Brazil, in company with Governor Jarvis, United States minister, I made an official call upon the Baron Cortegnpe, prime minister of the Empire. The minister informed me that Dr. Freire was absent and advised me to make the acquaintance of Dr. Aranjo Góes, a member of the central board of health, in whom the government had the utmost confidence. That Dr. Góes still enjoys the confidence of the government is shown by the fact that during the recent epidemic he was sent to Santos and to Campinas to establish hospitals and attend to the sanitary police of those cities.

It so happened that Dr. Góes was living in the same hotel in which I had established myself, and which was also the residence of the United States minister and the usual stopping place of Americans coming to the city of Rio. Naturally I hastened to make his acquaintance, and have every reason to congratulate myself upon having done so. "I found him to be an extremely well-informed physician, a competent microscopist, and one of the pioneers in Brazil in bacteriological studies, especially with reference to yellow fever. He has been prudent enough not to publish prematurely the results of his investigations, but has made extended experimental studies, and has especially devoted himself to the microscopical examination of sections of the various organs, made *secundum artem*, and stained with various aniline dyes." (Quoted from the introduction to my report, p. 142.)

In Dr. Freire's first publication upon the etiology of yellow fever he refers to Dr. Góes as follows:

These liquids, like the blood, the black vomit, the yellow vomit, the saliva, the pus, etc., constantly contain, as we have already said, innumerable microscopic

beings, which I have had occasion to show to physicians and distinguished specialists, among them Drs. Caminhoá, professor of the faculty of medicine, and Araujo Góes, professor of natural history, in the Imperial College of Pedro II. To this last confrère, *whose modesty equals his intelligence*, I present my thanks for his useful collaboration. (Recenil de Travaux Chimiques, etc., 1880, p. 266.)

Dr. Góes's scientific conservatism and "modesty" has prevented him from announcing any pseudo-discoveries, but has not prevented him from pointing out the errors and absurdities into which Dr. Freire has fallen and the unreliable character of his statistics. This he has done at the meetings of the Imperial Academy of Medicine, and his criticisms, which are upon record in the proceedings of the academy, show a truely scientific spirit, and in my opinion are well founded. This, I believe, is also the opinion of a majority of the members of the academy and of the best informed physicians in Rio.

Dr. Freire goes on to say:

In company with this gentleman, without my being informed, profiting by my absence, Dr. Sternberg has invaded the bacteriological laboratory of the faculty of medicine without the authority of the director of the faculty, and they have opened the closets in which were contained articles belonging to me, closets which I had left closed with a key which I had carried away with me. They have withdrawn the cultures which I had left there, because they were impure and of no value, etc.

This charge is simply untrue. I did, in company with Dr. Góes, call upon the director of the faculty of medicine, and this gentleman conducted me to the bacteriological laboratory and placed it at my disposal. That this is the fact he certainly will not deny, and my statement is supported by the letter of Dr. Góes, which I introduce below. In order to support his statement Dr. Freire publishes a document, signed by the secretary of the faculty, to the effect that "There does not exist in the office of the secretary of the faculty any document in virtue of which one can conclude that the director of the faculty, may have accorded to Drs. Francisco Marques de Araujo Góes and Dr. George Sternberg the permission to work in the section of bacteriology annexed to the laboratory of organic chemistry during the absence of the one asking the question—*du requérant*," being in response to a written question formulated by Dr. Freire.

The absence of such a written document is not surprising. I made no written request, and was conducted to the laboratory by the director of the faculty in person. That I would venture in a foreign city to invade without authority a closed laboratory in a building with which I was entirely unfamiliar, is too preposterous to demand attention were it not for the formal manner in which Dr. Freire has made the charge and the show of introducing documentary evidence, with which he has attempted to convince those who may read his pamphlet that I have been guilty of gross misconduct.

The second portion of the charge is equally untrue. Dr. Freire's two assistants, Dr. Chapot Prévost and Dr. Caminhoá, called upon me immediately after my arrival and offered me their services. My first visits to Dr. Freire's laboratory, after it was placed at my disposal by the director of the faculty, were made by appointment with these gentlemen, and one of them selected from the locked closets, of which he carried the key, the culture which I examined. Moreover I only mention incidentally the fact that these cultures were impure. I accepted the culture which Dr. Freire subsequently brought from Paris as an authentic culture of his yellow-fever microbe, and my conclusions relate to this micrococcus.

The following is a translation of Dr. Góes's reply to Dr. Freire's attack upon me, made in a medical congress held in the city of Rio, and subsequently repeated in his pamphlet referred to:

[Translation.]

To Dr. Domingos Freire:

Not being possible in the medical congress to continue a discussion which ceased to be scientific to become personal, I must use the public press to give a prompt reply to the discourse of Dr. Domingos Freire emitted yesterday. As for the insults which he heaped upon me, I will not repel them, for he who takes advantage of his position

which protects him from interruption, to insult an opponent bound by the regulations (of the congress) is neither a gentleman nor a polite man, consequently his insults can do me no harm; they can only injure himself. As to the scientific question, it is very true that Dr. Sternberg worked some fifteen or twenty days in June last year in the laboratory of Dr. Freire during his absence, by the authority of the director of the medical faculty; it is true that I went there some eight or ten times to assist Dr. Sternberg, and to try and learn something from him, because I consider him to be an expert in bacteriology; but it is false that either I or the American physician searched Dr. Freire's closets and lock-ups, and that we took advantage of his (Freire's) scientific processes to find out his secrets. As I have heretofore stated the only "culture" examined by us was furnished by Dr. Caminhoá Filho. Now, I wish to affirm that the only "lock-up" opened by order of Conselheiro Baron de Saboia was that which contained microscope slides, aniline colors, tubes, etc., the "lock-ups" with rotten cultures remaining locked, and we neither saw nor asked for the keys. I defy Dr. Freire to prove the contrary.

In this (following) point Dr. Freire spoke the truth. He himself confessed that all the there existing cultures were deteriorated, and in such cultures it is not possible to discover secrets, nor to find out scientific processes, *which could not be mysterious, as he himself described them in his publications.* Consequently, Dr. Freire, besides not speaking the truth, argued with his usual bad faith.

That which Dr. Freire hides, with the perfidy of a treacherous adversary, is that *Dr. Sternberg worked during the whole of July and ten days in August conjointly with Freire after his return from Europe; that he (Dr. Freire) fraudulently conceals that he himself showed Dr. Sternberg his "pure cultures," and performed himself his experiments and demonstrations in Dr. Sternberg's presence.* Note well that the American doctor was not idle, and in the absence of Dr. Freire he worked in the laboratory of the medical faculty, which belongs to the State, and where any one can work by permission of the authorities, and that as soon as Dr. Freire returned, they worked together. Now, I ask what is the motive of Dr. Freire, with such cunning in hiding this important fact, that is, *that he himself demonstrated his processes to Dr. Sternberg during thirty days in July and ten in August?* Because he wished to have it believed that the report of the illustrious American doctor was based *solely* on the examination of a deteriorated culture furnished spontaneously by his assistant, Dr. Caminhoá Filho.

This is false as false can be. Dr. Sternberg refers to the examination of a bad culture, but to draw his conclusions, contrary to Dr. Freire's wishes, he only used the demonstrations and experiments made in his presence by Dr. Freire himself after his return from Europe. Fixing myself on this point which can not be refuted, and can easily be proved by reading the report of the illustrious American physician, I ask who has given proofs of the want of scientific honesty and the want of morality.

Let the reader's good sense reply.

Dr. Freire accused me of having violated his laboratory. I have shown that I was there only with Dr. Sternberg, by order of the director of the faculty. He does not reply to this; hence I consider that he can not, and that he spoke falsely. He accused me of having violated his closets and furnishing Dr. Sternberg with deteriorated cultures. I have proved that the closets were locked, and that nobody touched them, and that the only culture examined was given by Dr. Caminhoá Filho. He did not reply to this; hence his accusation was considered false. What more is there in the two speeches of Dr. Freire in the medical congress? Trivialities and insults!

To conclude, two words as to the president of that congress: The Conselheiro president permitted Dr. Freire to insult me twice with impunity; the first time without notice, the second time his reprehension was so slight as to be entirely without effect. Consequently, I do not think I should again present myself at the meetings of the congress. I do not wish to be a passive victim of fresh insults.

ARAUJO GÓES.

RIO, 18*th September*, 1888.

Finally, Dr. Freire criticises my action in not making known the conclusions which I had reached as the result of my investigations while in Brazil, and in not attending the International Medical Congress in Washington for the purpose of publicly discussing the paper which I knew he was to read with reference to his preventive inoculations. There were several reasons for this action—first, my investigations were not completed, as my orders required me to go to Mexico and investigate the claims of Dr. Carmona y Valle, before making my report; second, I had no time to spare for the Washington meeting, as I was distinctly instructed to complete my investigations by the 1st of October; third, at the same time that I received my orders the following letter was placed in my hands, which I construed as meaning not only that I was required not to allow the publication of my instructions, but that I was expected to

refrain from publishing the results of my investigations until my report had been submitted to the President. Accordingly I refrained from making any publication, even in my address as President of the American Public Health Association at Memphis in November, 1887; and before making the summary statement in my address before the College of Physicians of Philadelphia in April, 1889, I called upon the President and obtained his permission to make public the results of my investigations in Brazil and in Mexico.

[Copy.]

TREASURY DEPARTMENT,
Washington, D. C., April 30, 1887.

DEAR SIR: It is the desire of the President that the inclosed instructions be not given to the press for publication until the report of Dr. Sternberg is made.

Yours, respectfully,

HUGH S. THOMPSON.

Supervising Surgeon-General JOHN B. HAMILTON, *Washington, D. C.*

Copy furnished for the information of Surgeon Sternberg.

APPENDIX.

As a matter of historical interest in connection with the subject of protective inoculations against yellow fever, I introduce here an account of the inoculations made in 1854 and 1855 by Dr. William Lambert de Humboldt, and those made in 1864 by Drs. Lebredo and Cisneros, of Havana.

Dr. de Humboldt claimed to be a nephew of the celebrated Alexander v. Humboldt. He asserted that he had discovered a sure means of protecting from yellow fever by inoculations with the venom of a poisonous snake, found in Mexico, but kept as a secret the precise species of snake from which his material for inoculations was obtained. His theory was based upon the fact that symptoms somewhat resembling those of yellow fever are produced by the venom of certain poisonous snakes. These symptoms are hemorrhage from the gums, slow pulse, fever, etc. The first experiments of Humboldt were made in Vera Cruz in 1847, by authority of the government, upon condemned prisoners. According to Boudin the matter inoculated was an ounce of sheep's liver which had been bitten by six of these poisonous serpents. This was left to undergo putrefaction before it was used for the inoculations.

A history of Humboldt's inoculations has been written by Dr. Nicolas B. L. Manzini. This is a volume of 240 pages, which was published in Paris in 1858. e shall quote from this work, which is entitled: "Histoire de l'inoculation préservative de la fièvre jaune, pratiquée par ordre du gouvernement espagnol, à l'hôpital militaire de la Havane." Rédigée par Nicolas B. L. Manzini, docteur en médecine de la Faculté de Paris, membre titulaire de la Société médicale d'émulation de Paris, médecin de l'Association de bienfaisance française de la Havane.

PREFACE.

However small the importance of our work may be it has cost us nevertheless two years of labor: the first, consecrated to making the inoculations, to taking notes, and treating the patients inoculated; the second, to writing it. * * * At the moment of printing it we ought to say that the only motive which has decided us to do so is to show that, contrary to the judgment of Dr. Bastarreche in his official report to the Spanish Government, the inoculations gave a good result during the year 1855, the first year of the experiment. The result of the years 1856 and 1857 is unknown to us; we await, in order to discuss it, a publication of the facts. Let it not be supposed from what we have said that we consider the inoculations to have been demonstrated to protect from yellow fever. We believe, on the contrary, that a question so complex could not be settled in a few months. * * * The hasty proscription of the inoculation, when 2,477 persons inoculated had only been followed by 67 deaths from yellow fever in the course of a year in place of 25 per cent of the number, which is the mean proportion of the mortality among troops arriving from Europe during the first year of their residence on this island; this proscription, we say, can prove nothing else than that the judgment had fallen upon persons who had not all the qualifications necessary to acquit themselves of this mission.

* * * * * * *

The circumstances which placed us in a position to write this history will appear in the proper place. * * * The delicate health of M. de Humboldt permitted us to practice nearly two thousand of the inoculations made and to treat nearly all of the fevers and other maladies of the inoculated, a care which M. de Humboldt very willingly intrusted to us. * * *

Since the end of the year 1855 there has been no further question of inoculation, and M. de Humboldt himself left Havana early in November 1856, having seen his discovery judged in a military way by a tribunal composed of a single individual and

executed with the precipitation of a state of siege. Finally the journals of Mexico, of the month of February, 1857, announced his death in Vera Cruz.

We do not inherit his secret, and we are ignorant whether or no he has left it to any one. * * * Let us not disturb the repose of the dead! And above all it is not for us to tear off his shroud for the purpose of ascertaining whether there was in him something other than the man of science. Certainly he had a rare intelligence, and was a person gifted with an extraordinary imagination, although his medical education was incontestably incomplete.

I take occasion in this preface to protest before the world of science against the reports which have been made with reference to the inoculations without knowledge of the facts. * * * There were only two individuals in a position to judge of them properly, M. Bastarreche and myself—M. Bastarreche by the official position which he occupied, and I by that which M. de Humboldt made for me.

Chapter I.

I. In the month of October, 1854, Dr. William Lambert de Humboldt, residing then in New Orleans, wrote to Gen. don José de la Concha, governor of the Island of Cuba, announcing to him that he had discovered a substance, the active principle of which was the venom of an ophidian, which substance, inoculated by vaccination in persons who were strangers in the localities where yellow fever reigns as an epidemic, protected them from this terrible malady. M de Humboldt said that during a period of nine years he had inoculated fourteen hundred and fifty-eight individuals. Of those whose history he had been able to follow he had only seen seven attacked with yellow fever, and of these only two had died. Out of three hundred and eighty-six inoculated in New Orleans he had not in any case seen yellow fever characterized by the pathognomonic symptoms—black vomit, etc. Finally, M. de Humboldt offered to apply his preservative to the Spanish troops of the Island of Cuba, in a most disinterested manner.

II. General Concha first consulted Dr. Basterreche, chief of the corps of military sanitation of the Island of Cuba, with reference to this important affair, who considered it prudent to consult with some of his medical friends, who all gave a favorable opinion. Then General Concha, who at the outset took a lively interest in the question, consulted, officially, the University, submitting at the same time a mémoir by M. de Humboldt relative to it. This corporation judged that the experiment was admissible and that the facts would decide the question. In consequence of this decision M. de Humboldt was invited to come to Havana. A ward in the military hospital was placed under his absolute direction. It was likewise agreed that all of the inoculated who should subsequently fall sick should be placed in his care, and that he could be assisted or replaced by persons of his selection. A commission of the University was named to follow the march of the operations and to make exact observations. It was composed of Drs. Cowley, Castroverde, and Benjumeda.

III. M. de Humboldt had scarcely arrived in Havana when I put myself in relations with him. He appears to be thirty-five to thirty-six years old. He is blonde, high and slender. His chest, flattened in front, offers the conformation peculiar to the tuberculous. * * * Although his health is precarious he is endowed with a feverish activity and with a resistance to work which is surprising. M. de Humboldt speaks four languages, among them the Spanish and French as perfectly as is possible for a foreigner. German is his native tongue and he speaks, besides, English. * * *

The special history of the phenomena of the inoculation which we are about to write is derived from seventy-nine observations collected and written out by M. de Humboldt and myself. Besides, we have drawn some information relative to the circulation and headache from one hundred and thirteen other cases, collected in the military hospital under the direction of M. de Humboldt.

We have little to say of the character of the substance inoculated, which has precisely the appearance and the odor of the liquid residue of animal putrefaction.

§1. *Local phenomena of the inoculation.*

As soon as the inoculation is made, a crossed bandage is applied to the puncture and no further attention is paid to it. If it is examined at the end of a few moments it will be found to be surrounded with an elevation in the form of a white papule, diaphanous, and quite analogous to that produced by the puncture of a bed-bug. This phenomenon was visible at the end of five minutes or even of three. It was no longer seen at the end of twenty-four hours, of twelve, or even of ten. A sensation of tingling and numbness, a veritable phenomenon of slight anesthesia, soon manifested itself in the fore-arm and lasted for a variable time; we have seen it persist until the fourth day in the case of Madame Mercedes Parodi. We have never seen any swelling of the axillary glands.

§2. *Outline of the sickness induced.*

Syncope may occur at the moment of inoculation, this soon passes; or a nervous trembling, which is more rare but which lasts longer. The pulse is accelerated under the influence of the emotion of the moment. At the end of seven hours (all of the times which follow are the mean time deduced from the extremes) the pulse is modified in a permanent manner; it is more frequent or slower, stronger or more feeble. At the end of eleven hours there is febrile heat; at the end of fourteen, headache, thirst, loss of appetite; at the end of sixteen the face is red, the conjunctivæ injected, lacrymation. A commencement of swelling of the gums is observed and slight colicky pains are experienced, produced by the medicine which the patient commenced to take immediately after the inoculation.

First. At the end of eighteen hours pain in the gums, which commence to be colored around the borders of the teeth; pain in the salivary glands and in the direction of the different nervous branches of the face and cranium. Second. Of nineteen hours, pains in the lower jaw in the direction of the inferior maxillary nerve, lassitude; of twenty hours, bitter taste, somnolence, œdema of the face; of twenty-two hours, feeling of constriction of the throat, without visible modification of the mucous membrane; of twenty-five hours, yellowness of the skin; of twenty-four hours, hemorrhage from the gums; of twenty-eight hours, eyes yellow, chills; of twenty-nine hours, inflammation of tonsils; of thirty hours, pain in region of kidneys; of thirty-six hours, œdema of eyelids; of thirty-eight hours, muscular and articular pains; of forty hours, toothache; of seventy-two hours, œdema of the lower lip; at different times, erotic phenomena. During convalescence, cutaneous itching; cutaneous eruptions of different kinds.

§3. *Immediate treatment.*

As soon as the inoculation was made we administered a sirup composed as follows:

℞. Sirop. de mikania guaco	187 gr.
Sirop. of rhubarbe	125 gr.
Iodure de potassium	4 gr.
Gomme gutte	12 gr.

D. et M.

This sirup was administered in the following manner: First day, a tablespoonful every two hours; second day, one every four hours; third day, one morning and evening. If the symptoms are more violent, the interval is shortened; and if that is not sufficient, it is necessary to add to the sirup an infusion of mikania,* a teacupful every two hours.

We shall not attempt to follow our author in his account of the symptoms produced by the poisons of various venomous snakes and in his attempt to show a resemblance between these symptoms and those of yellow fever. Nor shall we quote his account of the results of the inoculations made, inasmuch as we have these from an official source in the report of Dr. Bastarreche, which, with great fairness, Dr. Manzini has included in his volume, although he insists, contrary to the opinion and figures of Dr. Bastarreche, that the inoculations were attended with a comparatively favorable result.

EXTRACTS FROM THE OFFICIAL REPORT OF DR. M. BASTARRECHE, CHIEF OF THE CORPS OF MILITARY HYGIENE OF THE ISLAND OF CUBA.

The inoculations commenced the 18th of December among individuals who voluntarily presented themselves, the first having been Lieut. Col. M. Firmin Pujols, commandant of the engineers; after him some physicians of the army, other officers, and six soldiers, who, after the operation, which consisted in the introduction of the virus by means of a lancet, were subjected to the regimen indicated by Dr. Humboldt. This regimen consists in a moderate diet and in taking every two hours the sirup which had been prepared for this purpose: Sirup of a decoction of guaco, 350 grams; sirup of rhubarb, 225 grams; iodide of potassium, 4 grams, with the addition of 60 centigrams of gamboge dissolved in 16 grams of water. Of this sirup, which he ad-

* *Guaco, or huaco.*—Name in South America of several plants regarded as efficacious against the bites of venomous snakes. * * * (*Mikania guaco*, Humb. and Bonpland.) The juice from the interior is taken and applied to the wounds. The powder of guaco, which is also employed, has the appearance of that of digitalis and the odor of *semencontra* (Dict. of Nysten.).

ministered in doses of a teaspoonful, the patient took during the forty-eight hours as much as 500 grams, according to the symptoms which he presented.

In order that the observations might be made with the greatest impartiality and exactness, I detailed for this work a physician of the military service, M. Benoit Lozada y Astray, who established himself in the hospital, where he remained constantly, day and night, occupied continually with this difficult labor. * * * Since the day indicated new individuals were inoculated daily; experience having demonstrated that those who submitted to the operation were not exposed to any harm, the number augmented, and the commanding general of the navy, as well as the director of the congregation of Saint Vincent de Paul asked to have the sailors and the sisters of charity inoculated. The political events of February made it necessary to suspend the inoculations in consequence of the continual movements of troops and ships; they were again resumed, and finally suspended definitively when cholera invaded the military hospital, the accumulation of individuals being the most efficacious means of developing an epidemic, and especially in the military hospital, where so many elements are united favorable for such development, as has been observed on various occasions. The symptoms experienced by those inoculated varied in different cases. In many no noticeable result was seen; in others we observed slight chills and a temporary feeling of malaise; in other cases there was lassitude; others experienced pains in the joints; some pains in the back; and finally in some one observed in addition redness of the conjunctivæ, slowness of the pulse, swelling of the upper gums, and in a few rare cases a slight hemorrhage from the gums occurred. These symptoms commonly lasted for three or four days, and disappeared with the alvine discharges produced by the sirup, leaving the patient in a perfect state of health; no fatal accident occurred, although two thousand four hundred and seventy-seven individuals were inoculated in the military hospital. The physicians who composed the commission of the university having demanded from M. de Humboldt that he should give the sirup to some individuals who had not been subjected to the operation, in order to see whether the medicine did not contribute to the development of the symptoms presented by the patients, Dr. Humboldt opposed the proposition, and we were obliged to give up the experiment as well as the proposition to inoculate some animals, which was not accepted. Later Dr. de Humboldt demanded and obtained from the government permission to establish a place for the inoculation of the civil population who might wish to be inoculated, and as he received in such cases a pecuniary remuneration many persons commenced from this time to look upon him with suspicion; and, indeed, it was not without reason, for if the inoculation was a verity Dr. Humboldt would have been amply recompensed without having to employ any means to secure a reward.

When once a polemical discussion had been entered upon in the journals, several physicians, and some persons not belonging to the profession, joined in it. Disgusted with this, Dr. Humboldt demanded that the government should suspend the inoculations, a measure which was not adopted, for what was desired was to inoculate as large a number as possible, as a means of securing a prompt and decisive result. * * *

If we compare the number of individuals who entered the military hospital of Havana, attacked by yellow fever, in each of the months of the year 1854, with those of 1855 (see table No. 1) we observe that, as to the first months of summer, there were many less in the latter than in the former year, and even in the months of August, September, and October we see a great difference; that is to say, there were fewer cases in 1855; whether this was the effect of chance, or because the winter had been long and fresh, the fact is that until the time mentioned it seemed that the year was a favorable one in this respect, and for this reason those inoculated were attacked in small numbers. There was, therefore, no reason yet for drawing conclusions favorable or opposed to the solution of the question. But after the end of October, the season having been excessively warm, not only did yellow fever continue to prevail, but the number attacked was superior to that in 1854, and its intensity arrived at such a degree that the proportion of deaths to the number attacked was excessive. For this reason the commandant of the naval forces, in view of the great number of deaths, ordered that his sick, instead of being treated in the military hospital, should be taken to the *Maisons de Santé*, established in the port, upon the sea-board. In the communication which Dr. Humboldt sent to your excellency [the governor of the island to whom this report was made], dated October 27, was included a statistical statement, which showed that up to that time but nineteen of the inoculated had died of yellow fever; but in the twenty five days during which I delayed sending information to your excellency, in order to collect the facts with reference to this point, twenty-five of them died, which added to nineteen gives forty-four; from which it will be seen that the mortality was greater during this short period than during the entire summer. Attached to this report I submit to your excellency tables of the results, which show the number of cases of *vomito*, or yellow fever, which have

occurred in the army and in the navy. These tables have been made from all of those received from all of the military hospitals of the island, drawn up by the physicians of the army and by those of the navy (see tables 2, 3, and 4). In these tables the number of individuals is indicated who have had the disease in each of the hospitals of the island and in that of Havana, the corps to which they belong, the ship upon which they had embarked as sailors, as well as the mortality and the ratio per cent. The number of inoculated who have had the fever, and the number of deaths is also given. These facts prove clearly that no advantageous result has been obtained by inoculations of the virus proposed by Dr. Humboldt, but it is not less true that up to the present time no evil results have followed its application. May it not be that this inoculation, without preserving from the *vomito*, diminishes the probability of a fatal result in those attacked? In order to arrive at an exact judgment upon this question, it would be necessary to know what proportion the non-inoculated in the army bear to the two thousand four hundred and seventy-seven inoculated. But, independently of the fact that this is absolutely impossible, for it would be necessary to deduct those who have already been attacked, we can not start from this point since we must not include those who, by reason of long residence on the island may be considered acclimated and consequently can not enter into the comparison. Besides the different localities occupied by the troops necessarily influences the number of those attacked by the malady, for, as your excellency knows, there are localities where this cruel scourge augments considerably and others where it is scarcely known. Thus one can say nothing with regard to the difference between the number one thousand three hundred and nine attacked among the non-inoculated and two hundred and twenty-eight among the inoculated. Nor can we attach any importance to the greater mortality among the latter, which amounts to 29.39 per cent., while that of the first group is only 22.29 per cent. (see table No. 5). This difference may depend upon accidental circumstances, such, for example, as the greater or less salubrity of the localities of the hospitals where individuals of one or the other group have passed through the malady. The only fact worthy of attention is that which results from a comparison between the number inoculated and the number attacked with yellow fever, and between the latter and the number of deaths. The number inoculated was two thousand four hundred and seventy-seven, and the number attacked two hundred and twenty-eight, a proportion of 9.25 per cent. of the latter to the former number, while the ratio of deaths to those attacked is 2.70 per cent. If this number does not augment considerably in the following years, and if we had a point of departure for comparison with what happens in another group of soldiers not inoculated, we could yet, as a final observation, see if, considered in this way, the inoculations offer any appreciable value. This observation can be made by reason of the arrangement adopted by your excellency for examining the losses which have occurred during the past five years in the regiments of the king, of the queen, of Saragosse, and of Baylen, which, being new organizations, came to this island in 1851. And it will be proper in every way to keep an exact account of the losses which may occur among the inoculated, as your excellency has directed. This is all I have to say to your excellency relating to a question so interesting and most important for the soldiers, for humanity, and for science in general.

May God preserve your excellency for many years.

FERDINAND BASTARRECHE.

To His Excellency the Captain-General of the Island of Cuba.

HAVANA, *January* 25, 1856.

It will be sufficient to introduce here a single one of the tables appended to the report of Dr. Bastarreche.

COMPARATIVE SUMMARY.

Table No. V.

	Not inoculated.			Inoculated.			Ratio of mortality.
	Attacked.	Died.	Ratio.	Number.	Attacked.	Died.	
Army	1,045	254	24.31	1,214	84	21	25.00
Navy	264	47	17.80	1,263	144	46	31.94
Total	1,309	301	22.99	2,477	228	67	29.39

Nothing further has been heard of Dr. Humboldt's method of inoculation in Havana, and the inference is that by common consent the experiment made on so large a scale and under such favorable conditions is regarded as having demonstrated its inutility.

A more recent attempt to protect from yellow fever by inoculation is that made in 1864 by two physicians of Havana, members of the Academy of Sciences, and recorded in the "Anales" of the Academy. We quote the translation which Dr. Stanford E. Chaillé, president of the Havana Yellow Fever Commission of the National Board of Health, has introduced into his elaborate and valuable report: *

In June, 1864, Drs. Lebredo and Cisneros, members of the academy, and distinguished physicians, tested the prophylactic value of inoculated dew, by request of Drs. Masnata and Fraschieri, who had claimed for it protective power.

The substance used was not, as had been generally supposed, natural dew, but an artificial dew obtained by the condensation of vapor of the atmosphere of the closed room of a yellow fever patient, and collected on the surface of bottles containing water of a lower temperature than that of the surrounding air. After prolonged examination the following were our conclusions:

Yellow fever is not a contagious nor an inoculable disease, hence the inoculation of dew can not be effective. There is no such entity as the so-called "fever of acclimation," and it has not been proved that the ailments thus designated protect from yellow fever. The symptoms following the inoculation of "rocio" lack the uniformity necessary to constitute a classifiable pathological condition as dependent solely on the inoculation; the very slight intensity of the phenomena discredit their identity with those of the so-called "fever of acclimation;" in many instances no phenomena have ensued, and all the results obtained are explicable by disregard of hygienic laws. In three counter-experiments distilled water was inoculated. In one case more remarkable results ensued than in any case inoculated with "rocio;" in a second the results were as mild, and in a third case no results at all ensued. Finally, as the result of experiments, the inoculation of "rocio" is ineffective, and equally as negative as inoculations of black and of bilious vomit.

* Annual Report of the National Board of Health for 1880, p. 166.